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TRANSACTIONS

OF THE

CONGRESS

OF

American Physicians and Surgeons.

FOURTH TRIENNIAL SESSION,

HELD AT

WASHINGTON, D. C.

May 4th, 5th and 6th, 1897.

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EXTRACT FROM THE MINUTES OF THE EXECUTIVE COMMITTEE.

At a meeting of the Executive Committee held November 23d, 1895, it was moved by Dr. Taylor and carried:—"That the precedent established in 1894 [for the arrangement of discussions before the Congress] be adopted for the Congress of 1897" for the remaining Societies.

Under this resolution the following Societies and Associations were assigned to prepare subjects and persons for the discussions.

1st. The American Ophthalmological Society.
2d. The American Otological Society.
3d. The American Orthopedic Association.
4th. The Association of American Physicians.
5th. The American Physiological Society.
6th. The American Pediatric Society.
7th. The American Surgical Association.

MINUTES.

The fourth triennial session of the CONGRESS OF AMERICAN PHYSICIANS AND SURGEONS took place in Washington, D. C., on May 4th, 5th and 6th, 1897.

A business meeting of the Congress was held in the Columbia Theater, corner of Twelfth and F streets, N. W.; it was called to order at 1.30 P. M. by the President.

DR LANDON CARTER GRAY, Chairman of the Executive Committee, opened the Congress. He said:—

Ladies and Gentlemen:

Any well-wisher of this body, familiar with its unwritten history, may be pardoned for feeling a glow of satisfaction at the sight of the great programme offered to us; evidencing, as it does, not only the generous coöperation of the constituent associations, but also a mental activity holding its own in the keen competition of the modern medical congress. Certainly to me it is a very great pleasure to open this, the fourth Congress of American Physicians and Surgeons, and to go through the formality of introducing to you the distinguished gentleman whom we all love to honor, Dr. William H. Welch, of Baltimore, our President.

DR. W. H. WELCH, Baltimore:—Mr. Chairman and Gentlemen, I shall follow the example of my predecessors in office and not seize this opportunity for making an address. My time for that comes to-morrow night. The success of the Congress depends upon its scientific work, and all I shall do at present is to express my great thanks for the honor conferred upon me, and to express my thanks to the officers who have done so much in arranging the programme to make it a success. We will proceed at once to the business of the Congress.

This business meeting is called in accordance with a resolution adopted at the last meeting of the Congress. I will ask the Chairman of the Executive Committee to state that business.

DR. L. C. GRAY:—The business relates to the change of place of holding the Congress. At the last session Dr. White moved to strike out Washington as the place of meeting and to give the

Executive Committee the power to determine where it should be held. Dr. Busey then moved that the consideration of Dr. White's motion be postponed and made the special order for the first day's session of the next Congress, and that is the question now before you for consideration.

Dr. Mastin:—I move the question be laid upon the table.

Dr. Busey:—I second the motion.

Dr. Carmalt:—Does that dispose of the subject *in toto*, or may it come up again at some future meeting?

Dr. Busey:—Allow me to say that a motion to lay upon the table disposes of the matter finally, except that to reconsider it requires a two-thirds vote. It disposes of it for all time unless a two-thirds vote is given for reconsideration.

The question was put on the motion to lay on the table and the President declared it carried.

Dr. Busey:—I now move you, Mr. President, that we reconsider the motion to lay upon the table, and that we lay the motion to reconsider on the table.

This motion was seconded and adopted by vote of the Congress.

Dr. Roberts, Phila.:—I would offer the following resolution: "That for the next and all subsequent Congresses the Executive Committee be requested to make provision for reduced railroad rates."

The motion was seconded and adopted.

Dr. Busey:—Shall we have any time for further business?

The President:—Our time has not expired.

Dr. Busey:—I did not anticipate it would come up this afternoon, and, therefore, did not bring the papers with me, but I am instructed by the Joint Committee on Vivisection, composed of representatives of the scientific societies of this city, to report to this body that the bill that has been before the Senate for more than a year, and was unanimously reported favorably last year, has again been reported favorably to the Senate, under a different number. The Joint Committee on Vivisection has presented two protests against the passage of that bill to the last session of the last Congress, and we have reason to believe that those protests secured its delay, but in the many changes that have occurred in the Senate we have lost some of our best friends. I do not know that those who have taken their places are our enemies; we have not had time to determine that. We addressed a letter to the chairman of the committee in charge of this subject, requesting the

opportunity to be heard before the whole committee before the question was finally decided. I have a letter from Mr. McMillan in which he simply says: "Your letter has been referred to Senator Gallinger," and there the matter ends. We are in apprehension every day that this matter will be called up before the Senate, and that when called up it will pass that body. We were quite sure that it could not pass the last Congress because it could not be taken up without unanimous consent, but we are not sure that such is the case now.

I suggest that we appoint a committee to present its protest to Congress, and not only ask to be heard, but that it have time and opportunity to be heard fully. Those opposed to this legislation have never had the opportunity to be heard as they desire. They have had opportunities, but they were such as this: A telephone message at 2 o'clock to be at the Senate at 2.30. If a body like this shall present its remonstrance against the passage of the bill, coupled with a request that it shall be fully heard by its representatives, we feel that it will accomplish a great deal.

THE PRESIDENT:—How shall the committee be appointed?

DR. BUSEY:—By the chair.

DR. STERNBERG:—I would suggest that the committee to be appointed shall consist of a member from each constituent society and not a resident of Washington. I would say in regard to our opportunities to be heard that I was summoned one day to be present at the Senate within an hour, and another member of the committee, I think, had only fifteen minutes notice.

DR. BUSEY:—A remonstrance, written or verbal, coming from residents of the country outside of the District of Columbia, who are voters and a power in elections, is worth more than anything we can do; I should say that one such letter is worth more than all our efforts. We are without votes and without influence, whereas a member from Massachusetts, or elsewhere, will bring to bear a power that the whole population of the District of Columbia cannot.

DR. STERNBERG:—I think probably Dr. Busey intended to include that the committee was not simply to prepare resolutions and send them, for we have had any quantity of them. We have strong resolutions on file now, but Senators have not the time to read such things. They should have a great weight, but when they get before the Senate it is doubtful whether they are read by any considerable number. This committee should be organized to do something further.

THE PRESIDENT:—I think the committee should be authorized to take any further steps they may think necessary to bring about the desired results.

Dr. Busey's motion was unanimously adopted.

DR. S. S. ADAMS, Chairman of the Committee of Arrangements:—The meeting to-morrow afternoon will be held at the National Theater. The Cosmos Club extends the privileges of the club to members of this Congress and also invites them to a "smoker" at its club rooms, corner of H street and Vermont avenue, on Thursday evening.

THE PRESIDENT:—The business of the Congress being now concluded, and the time appointed for the general meeting having arrived, it will be held under the direction of THE AMERICAN OPHTHALMOLOGICAL SOCIETY, the subject being "The Gouty and Rheumatic Diatheses, and their Relation to Diseases of the Eye." The first paper will be by Dr. Chas. S. Bull, of New York, on "Lesions of the Vessels of the Retina and Optic Nerve Associated with Gout" (page 1). Dr. Bull was followed by Dr. Samuel D. Risley, of Philadelphia, with a paper on "Cataract and its Association with the Gouty and Rheumatic Diatheses" (page 8). Dr. Stephen O. Richey, of Washington, D. C., then read a paper on "Gout and Rheumatism in the Etiology of Glaucoma" (page 16); and Dr. Robert Sattler, of Cincinnati, Ohio, on "The Gouty and Rheumatic Affections of the Uveal Tract" (page 27); and Dr. R. A. Reeve, of Toronto, Canada, on "The Gouty and Rheumatic Affections as Involving the Conjunctiva, Cornea and Sclera" (page 41). After which Dr. J. M. DaCosta, of Philadelphia, spoke in discussion (page 49).

At 3.30 P. M., THE AMERICAN OTOLOGICAL SOCIETY took charge of the meeting with a paper by Dr. Clarence J. Blake, of Boston, on "Otology in its relation to General Medicine" (page 53).

THE PRESIDENT:—This is the first time that a general address has been given in place of a discussion, and I believe we have had exemplified here the feasibility of that procedure. I think that I express the sentiments of all present in thanking Dr. Blake for his address.

This meeting is now adjourned.

The second general meeting of the Congress was held on Wednesday, May 5th, at 2 P. M., in the New National Theater.

THE PRESIDENT said:—This is the only session that is to be held in this theater. The address this evening and future meetings will be in the New Columbia Theater. It is important that these

exercises should not close later than 4.45 P. M., in order that we may attend the exercises of the unveiling of the Gross monument.

THE PRESIDENT then announced that this meeting was held under the joint participation of THE ASSOCIATION OF AMERICAN PHYSICIANS, THE AMERICAN PHYSIOLOGICAL SOCIETY and THE AMERICAN PEDIATRIC SOCIETY, and the subject for discussion to be "Internal Secretions Considered in Their Physiological, Pathological and Clinical Aspects."

The first paper was by Dr. W. H. Howell, of Baltimore, Md., on "The Physiology of the Internal Secretions" (page 70), read by Dr. F. S. Lee. It was followed by a paper by Prof. R. H. Chittenden, of New Haven, Conn., on "The Internal Secretions Considered from a Chemico-Physiological Standpoint" (page 87). Dr. J. George Adami, of Montreal, Canada, then read a paper on "The Doctrine of the Internal Secretory Activity of Glands in Relation to the Pathological Anatomy of Sundry Morbid Conditions" (page 103). Dr. James J. Putnam, of Boston, read a paper on "The Internal Secretions Considered in some of Their Clinical Aspects" (page 122), and Dr. Francis P. Kinnicutt, of New York, on "The Therapeutics of the Internal Secretions" (page 144); and Dr. Wm. Osler, of Baltimore, Md., concluded the meeting with remarks on Sporadic Cretinism in America, illustrated by photographs exhibited by a stereopticon. (Paper on page 169.)

The meeting then adjourned.

The third general meeting was held in the evening of Wednesday, May 5th, at 8.30 P. M., to listen to THE ADDRESS OF THE PRESIDENT OF THE CONGRESS, Dr. William H. Welch, Professor of Pathology in Johns Hopkins University. Dr. Arthur Mathewson, President of THE AMERICAN OTOLOGICAL SOCIETY, *ex-officio* First Vice-President, in the chair.

Dr. Welch's address was on Adaptation in Pathological Processes (page 284).

The fourth general meeting of the Congress was held on Thursday, May 6th, at 2 P. M., in the New Columbia Theater. The President announced that the Congress, until 3.30 P. M., would be under the direction of THE AMERICAN ORTHOPEDIC ASSOCIATION.

A paper was read by Dr. E. H. Bradford, of Boston, Mass., on "Deformities of the Hip-Joint, especially Congenital Dislocations" (page 207).

The paper was discussed by Dr. V. P. Gibney, of New York, (page 231); and Dr. Harry M. Sherman, of San Francisco, Cal. (page 233).

At 3.30 P. M., the meeting became under the direction of THE AMERICAN SURGICAL ASSOCIATION, the subject being "The Classification, Prognosis and Treatment of Acute General Peritonitis." The first paper was read by Dr. Nicholas Senn, of Chicago, Ill., on the "Classification of Acute General Peritonitis" (page 237). Dr. Robert Abbe, of New York, then read a paper on "The Prognosis and Treatment of the Different Varieties" (page 254). He was followed in discussion with papers by Dr. A. J. McCosh, of New York, (page 266); and Dr. George R. Fowler, of Brooklyn, L. I., (page 270); and remarks by Dr. W. H. Welch, Dr. Abbe, Dr. J. Taber Johnson and Dr. McCosh in reply to enquiry as to method of injection of Epsom salt solution (page 283).

At the end of the discussion, the fourth triennial session of the Congress being about to close, the SECRETARY moved: That, in view of the courtesies so hospitably offered us by the Comos Club, of Washington, D. C., a vote of thanks be given them from the Congress.

Seconded by Dr. Abbe and unanimously adopted.

The PRESIDENT, Dr. Welch, then said:—In closing, I think we have many reasons to feel gratified. We have had the exceptional experience of pleasant weather. The registration is very much over 500, and a considerable number are in attendance who have not placed their names on the rolls. The programmes for the special societies have been unusually full and rich, and the general discussions before the Congress have been, I think, excellent. The papers have all been of a high order and will make a notable collection. I wish to express my personal thanks for the coöperation received on all sides in duties with which I had no familiarity.

I now announce the fourth Congress closed.

GUESTS OF THE CONGRESS.

Brig. General George M. Sternberg, M.D., LL.D., Surgeon General United States Army.

Surgeon General J. Rufus Tryon, Chief of Bureau of Medicine and Surgery, United States Navy.

Walter Wyman, M.D., Supervising Surgeon General of the United States Marine Hospital Service.

MEMBERS OF THE CONGRESS.

Members present are indicated by *.

AMERICAN OPHTHALMOLOGICAL SOCIETY.

Organized, June, 1864.

ACTIVE MEMBERS.

Dr. F. W. Abbot,	Buffalo, New York.
*Dr. A. E. Adams,†	Newburgh, New York.
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Dr. Niel J. Hepburn,	New York City.
Dr. Ward Holden,†	New York City.
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Dr. J. P. Worrell,	Terre Haute, Indiana.

†Associate Members.

HONORARY MEMBER.

Dr. C. Schweigger,	Berlin, Germany.

AMERICAN OTOLOGICAL SOCIETY.

Organized, July, 1866.

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*Dr. F. M. Wilson,	Bridgeport, Connecticut.

†Associates.

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Prof. Alfred M. Mayer,	Hoboken, New Jersey.
Mr. William MacEwen,	Glasgow, Scotland.
Prof. Adam Politzer,	Vienna, Austria.
Prof. Ogden M. Rood,	New York City.

AMERICAN NEUROLOGICAL ASSOCIATION.

Organized, June, 1875.

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Dr. Henry Hun,	Albany, New York.
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AMERICAN GYNECOLOGICAL SOCIETY.

Organized, June, 1876.

ACTIVE FELLOWS.

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Dr. E. W. Schauffler,	Kansas City, Missouri.
Dr. Henry H. Schroeder,	New York City.
Dr. E. L. Shurly,	West Detroit, Michigan.
*Dr. A. Alexander Smith,	New York City.
Dr. Andrew H. Smith,	New York City.
Dr. Frank Fremont Smith,	St. Augustine, Florida.
*Dr. S. E. Solly,	Colorado Springs, Colorado.
Dr. H. Longstreet Taylor,	St. Paul, Minnesota.
*Dr. J. Madison Taylor,	Philadelphia, Pennsylvania.
Dr. J. Carey Thomas,	Baltimore, Maryland.
Dr. E. L. Trudeau,	Saranac Lake, New York.
Dr. J. Hilgard Tyndale,	Lincoln, Nebraska.
*Dr. J. B. Walker,	Philadelphia, Pennsylvania.
Dr. Samuel B. Ward,	Albany, New York.
Dr. E. W. Watson,	Philadelphia, Pennsylvania.
Dr. Leonard Weber,	New York City.
Dr. H. H. Whitcomb,	Norristown, Pennsylvania.
Dr. H. F. Williams,	Brooklyn, New York.
*Dr. James C. Wilson,	Philadelphia, Pennsylvania.

HONORARY MEMBERS.

Dr. Alfred Stillé,	Philadelphia, Pennsylvania.
Dr. Hermann Weber,	London, England.
Dr. Charles Theodore Williams,	London, England.

ASSOCIATION OF AMERICAN PHYSICIANS.

Organized, October, 1885.

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*Dr. John J. Abel,	Baltimore, Maryland.
*Dr. J. George Adami,	Montreal, Canada.
*Dr. J. F. A. Adams,	Pittsfield, Massachusetts.
*Dr. Isaac Adler,	New York City.
*Dr. I. E. Atkinson,	Baltimore, Maryland.
*Dr. A. Brayton Ball,	New York City.
Dr. G. Baumgarten,	St. Louis, Missouri.
*Dr. Herman M. Biggs,	New York City.
*Dr. Frank Billings,	Chicago, Illinois.
Dr. B. Meade Bolton,	Columbia, Missouri.
Dr. Chas. S. Bond,	Richmond, Indiana.
*Dr. Norman Bridge,	Los Angeles, California.
*Dr. Samuel C. Busey,	Washington, D. C.
*Dr. Charles Cary,	Buffalo, New York.
*Dr. W. T. Councilman,	Boston, Massachusetts.
Dr. Arthur C. Cushney,	Ann Arbor, Michigan.
*Dr. Elbridge G. Cutler,	Boston, Massachusetts.
*Dr. J. M. Da Costa,	Philadelphia, Pennsylvania.
*Dr. Chas. L. Dana,	New York City.
Dr. Israel T. Dana,	Portland, Maine.
Dr. I. N. Danforth,	Chicago, Illinois.
*Dr. Francis Delafield,	New York City.
*Dr. George Dock,	Ann Arbor, Michigan.
*Dr. Wm. H. Draper,	New York City.
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Dr. Harold C. Ernst,	Jamaica Plain, Massachusetts.
*Dr. Samuel A. Fisk,	Denver, Colorado.
*Dr. Reginald H. Fitz,	Boston, Massachusetts.
Dr. W. E. Fischel,	St. Louis, Missouri,
*Dr. Simon Flexner,	Baltimore, Maryland.
Dr. Charles F. Folsom,	Boston, Massachusetts.
Dr. F. Forchheimer,	Cincinnati, Ohio.
*Dr. M. Howard Fussell,	Philadelphia, Pennsylvania.
Dr. George M. Garland,	Boston, Massachusetts.
Dr. J. E. Graham,	Toronto, Canada.
*Dr. J. P. Crozer-Griffith,	Philadelphia, Pennsylvania.
*Dr. John Guiteras,	Philadelphia, Pennsylvania.
*Dr. Hobart A. Hare,	Philadelphia, Pennsylvania.
*Dr. I. Minis Hays,	Philadelphia, Pennsylvania.
Dr. Ludwig Hektoen,	Chicago, Illinois.
Dr. Frederick P. Henry,	Philadelphia, Pennsylvania.
*Dr. Henry Hun,	Albany, New York.
*Dr. Henry Mills Hurd,	Baltimore, Maryland.

*Dr. A. Jacobi,	New York City.
*Dr. E. G. Janeway,	New York City.
*Dr. W. W. Johnston,	Washington, D. C.
*Dr. Francis P. Kinnicutt,	New York City.
*Dr. Henri A. Lafleur,	Montreal, Canada.
Dr. Thomas S. Latimer,	Baltimore, Maryland.
Dr. Morris J. Lewis,	Philadelphia, Pennsylvania.
Dr. Morris Longstreth,	Philadelphia, Pennsylvania
Dr. Starling Loving,	Columbus, Ohio.
Dr. Henry M. Lyman,	Chicago, Illinois.
*Dr. A. McPhedran,	Toronto, Canada.
*Dr. A. Lawrence Mason,	Boston, Massachusetts.
Dr. Arthur V. Meigs,	Philadelphia, Pennsylvania
*Dr. S. J. Meltzer,	New York City.
Dr. S. Weir Mitchell,	Philadelphia, Pennsylvania.
*Dr. John H. Musser,	Philadelphia, Pennsylvania.
*Dr. W. P. Northrup,	New York City.
*Dr. Wm. Osler,	Baltimore, Maryland.
*Dr. George L. Peabody,	New York City.
Dr. William Pepper,	Philadelphia, Pennsylvania.
Dr. Wm. M. Polk,	New York City.
*Dr. D. W. Prentiss,	Washington, D. C.
*Dr. T. Mitchell Prudden,	New York City.
*Dr. James J. Putnam,	Boston, Massachusetts.
*Dr. B. K. Rachford,	Cincinnati, Ohio.
*Dr. Walter Reed,	Washington, D. C.
*Dr. Beverley Robinson,	New York City.
*Dr. T. M. Rotch,	Boston, Massachusetts.
Dr. Edward O. Shakespeare,	Rosemont, Pennsylvania.
*Dr. Frederick C. Shattuck,	Boston, Massachusetts.
*Dr. George B. Shattuck,	Boston, Massachusetts.
*Dr. Wharton Sinkler,	Philadelphia, Pennsylvania
*Dr. A. A. Smith,	New York City.
Dr. Andrew H. Smith,	New York City.
Dr. Theobald Smith,	Jamaica Plain, Massachusetts.
*Dr. Louis Starr,	Philadelphia, Pennsylvania.
*Dr. M. Allen Starr,	New York City.
*Dr. Geo. M. Sternberg, U. S. A.,	Washington, D. C.
*Dr. D. D. Stewart,	Philadelphia, Pennsylvania.
*Dr. James Stewart,	Montreal, Canada.
*Dr. Charles G. Stockton,	Buffalo, New York.
Dr. W. S. Thayer,	Baltimore, Maryland.
*Dr. W. Gilman Thompson,	New York City.
Dr. Wm. H. Thomson,	New York City.
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Dr. Ira T. Van Gieson,	New York City.
Dr. V. C. Vaughan,	Ann Arbor, Michigan.
Dr. Henry P. Walcott,	Cambridge, Massachusetts.
Dr. Samuel B. Ward,	Albany, New York.

*Dr. Wm. H. Welch,	Baltimore, Maryland.
*Dr. James T. Whittaker,	Cincinnati, Ohio.
*Dr. George Wilkins,	Montreal, Canada.
*Dr. Francis H. Williams,	Boston, Massachusetts.
*Dr. James C. Wilson,	Philadelphia, Pennsylvania.
*Dr. Horatio C. Wood,	Philadelphia, Pennsylvania.

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Dr. J. S. Billings, U. S. A.,	New York City.
Dr. Samuel C. Chew,	Baltimore, Maryland.
Dr. Meredith Clymer,	New York City.
Dr. John T. Metcalfe,	Garrisons, New York.
Dr. F. T. Miles,	Baltimore, Maryland.
Dr. Francis Minot,	Boston, Massachusetts.
Dr. Alfred Stillé,	Philadelphia, Pennsylvania.

AMERICAN ASSOCIATION OF GENITO-URINARY SURGEONS.

Organized, October, 1886.

ACTIVE MEMBERS.

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Dr. Gardner W. Allen,	Boston, Massachusetts.
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Dr. Charles F. Bevan,	Baltimore, Maryland.
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Dr. F. Tilden Brown,	New York City.
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*Dr. Edwin C. Burnett,	St. Louis, Missouri.
*Dr. Arthur T. Cabot,	Boston, Massachusetts.
Dr. N. B. Carson,	St. Louis, Missouri.
*Dr. George Chismore,	San Francisco, California.
Dr. H. M. Christian,	Philadelphia, Pennsylvania.
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Dr. John A. Fordyce,	New York City.
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Dr. W. F. Glenn,	Nashville, Tennessee.
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Dr. Ramon Guitéras,	New York City.
*Dr. J. R. Hayden,	New York City.
Dr. Wm. H. Hingston,	Montreal, Canada.
Dr. Orville Horwitz,	Philadelphia, Pennsylvania.
Dr. J. Nevins Hyde,	Chicago, Illinois.
*Dr. Wm. Judkins,	Cincinnati, Ohio.
Dr. Edward L. Keyes,	New York City.

Dr. E. E. King,	Toronto, Canada.
*Dr. Bransford Lewis,	St. Louis, Missouri.
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*Dr. Harvey G. Mudd,	St. Louis, Missouri.
Dr. Fessenden N. Otis,	New York City.
*Dr. W. K. Otis,	New York City.
Dr. Roswell Park,	Buffalo, New York.
Dr. Abner Post,	Boston, Massachusetts.
Dr. Charles L. Scudder,	Boston, Massachusetts.
Dr. Alexander W. Stein,	New York City.
*Dr. Frederick R. Sturgis,	New York City.
Dr. George K. Swinburne,	New York City.
*Dr. Robert W. Taylor,	New York City.
*Dr. Paul Thorndike,	Boston, Massachusetts.
*Dr. James P. Tuttle,	New York City.
Dr. John Van der Poel,	New York City.
*Dr. Francis S. Watson,	Boston, Massachusetts.
*Dr. J. Wm. White,	Philadelphia, Pennsylvania.
*Dr. J. Blake White,	New York City.
Dr. W. N. Wishard,	Indianapolis, Indiana.

AMERICAN ORTHOPEDIC ASSOCIATION.

Organized, May, 1887.

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*Dr. Wallace Blanchard,	Chicago, Illinois,
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*Dr. Dillon Brown,	New York City.
Dr. Joseph D. Bryant,	New York City.
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Dr. C. C. Foster,	Cambridge, Massachusetts.
*Dr. V. P. Gibney,	New York City.
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*Dr. Joel E. Goldthwaite,	Boston, Massachusetts.
*Dr. J. D. Griffith,	Kansas City, Missouri.
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Dr. James E. Moore,	Minneapolis, Minnesota.
Dr. T. Halstead Myers,	New York City.
Dr. George B. Packard,	Denver, Colorado.
Dr. Roswell Park,	Buffalo, New York.
Dr. A. M. Phelps,	New York City.
Dr. W. O. Plympton,	New York City.
*Dr. John Ridlon,	Chicago, Illinois.
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*Dr. John C. Schapps,	Pueblo, Colorado.
*Dr. C. L. Scudder,	Boston, Massachusetts.
*Dr. Newton M. Shaffer,	New York City.
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*Dr. Harry M. Sherman,	San Francisco, California.
*Dr. A. J. Steele,	St. Louis, Missouri.
*Dr. Henry Ling Taylor,	New York City.
*Dr. R. T. Taylor,	Baltimore, Maryland.
*Dr. Wm. J. Taylor,	Philadelphia, Pennsylvania.
Dr. Augustus Thorndike	Boston, Massachusetts.
*Dr. W. R. Townsend,	New York City.
Dr. L. A. Weigel,	Rochester, New York.
Dr. R. Whitman,	New York City.
*Dr. DeForest Willard,	Philadelphia, Pennsylvania.
*Dr. H. Augustus Wilson,	Philadelphia, Pennsylvania.
Dr. W. E. Wirt,	Cleveland, Ohio.
Dr. James K. Young,	Philadelphia, Pennsylvania.

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Dr. Henry G. Davis,	Everett, Massachusetts.
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Dr. Lannelongue,	Paris, France.
Wm. J. Little, Esq.,	Ryarsh, Kent, England.
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Dr. Leopold Ollier,	Lyons, France.
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Dr. F. Beely,	Berlin, Germany.
M. Bilhaut,	Paris, France.
Nicholas Grattan, Esq.,	Cork, Ireland.
Dr. A. Hoffa,	Würzburg, Germany.
Robert Jones, Esq.,	Liverpool, England.

Dr. E. Kermisson,	Paris, France.
Dr. Sigfred Levy,	Copenhagen, Denmark.
Ernst Muirhead Little, Esq.,	London, England.
Dr. Adolf Lorenz,	Vienna, Austria.
Howard Marsh, Esq.,	London, England.
Edmund Owen, Esq.,	London, England.
Pietro Panzeri,	Milan, Italy.
Robert Wm. Parker, Esq.,	London, England.
Dr. Paul Redard,	Paris, France.
Bernhard Roth, Esq.,	London, England.
Noble Smith, Esq.,	London, England.
W. J. Walsham, Esq.,	London, England.
George Arthur Wright,	Manchester, England.
Dr. Julius Dollinger,	Buda-Pesth, Austro-Hungary.

AMERICAN PHYSIOLOGICAL SOCIETY.

Organized, December, 1887.

ACTIVE MEMBERS.

*Dr. Alexander C. Abbott,	Philadelphia, Pennsylvania.
*Dr. J. J. Abel,	Baltimore, Maryland.
*Dr. J. George Adami,	Montreal, Canada.
*Dr. Thomas B. Aldrich,	Baltimore, Maryland.
Dr. H. G. Beyer, Surg., U. S. N.,	Annapolis, Maryland.
*Dr. H. P. Bowditch,	Boston, Massachusetts.
Dr. Leo Breisacher,	Detroit, Michigan.
*Dr. A. P. Brubaker,	Philadelphia, Pennsylvania.
Dr. J. P. Campbell,	Athens, Georgia.
Dr. Wm. S. Carter,	Philadelphia, Pennsylvania.
*Dr. J. McK. Cattell,	Garrison-on-Hudson, New York.
Dr. H. C. Chapman,	Philadelphia, Pennsylvania.
*Prof. R. H. Chittenden,	New Haven, Connecticut.
Dr. Gaylord P. Clark,	Syracuse, New York.
Dr. W. T. Councilman,	Boston, Massachusetts.
Dr. Richard H. Cunningham,	New York City.
Dr. J. G. Curtis,	New York City.
*Dr. A. R. Cushney,	Ann Arbor, Michigan.
Dr. H. H. Donaldson,	Chicago, Illinois.
*Dr. G. P. Dreyer,	Baltimore, Maryland.
Dr. F. W. Ellis,	Monson, Massachusetts.
Dr. George W. Fitz,	Cambridge, Massachusetts.
Dr. G. L. Goodale,	Cambridge, Massachusetts.
*Dr. H. A. Hare,	Philadelphia, Pennsylvania.
Dr. C. F. Hodge,	Worcester, Massachusetts.
Dr. Theodore Hough,	Boston, Massachusetts.
Dr. W. H. Howell,	Baltimore, Maryland.
*Dr. G. Carl Huber,	Ann Arbor, Michigan.

Dr. Reid Hunt,	New York City.
*Dr. G. T. Kemp,	Baltimore, Maryland.
*Dr. F. S. Lee,	New York City.
Dr. Phoebus A. Levene,	New York City.
Dr. Frank Spiller Locke,	Boston, Massachusetts.
Dr. Jacques Loeb,	Chicago, Illinois.
Dr. W. P. Lombard,	Ann Arbor, Michigan.
*Dr. Graham Lusk,	New Haven, Connecticut.
Dr. A. B. Macallum,	Toronto, Canada.
*Dr. F. P. Mall,	Baltimore, Maryland.
Dr. John Marshall,	Philadelphia, Pennsylvania.
Dr. Lafayette B. Mendel,	New Haven, Connecticut.
*Dr. S. J. Meltzer,	New York City.
Dr. W. Mills,	Montreal, Canada.
Dr. C. S. Minot,	Boston, Massachusetts.
Dr. S. Weir Mitchell,	Philadelphia, Pennsylvania.
Dr. G. F. H. Nuttall,	Berlin, Germany.
*Dr. Wm. Osler,	Baltimore, Maryland.
Dr. Isaac Ott,	Philadelphia, Pennsylvania.
*Dr. Franz Pfaff,	Boston, Massachusetts.
*Dr. Wm. Townsend Porter,	Boston, Massachusetts.
Dr. Edward T. Reichert,	Philadelphia, Pennsylvania.
Dr. W. T. Sedgwick,	Boston, Massachusetts.
Dr. Henry Sewall,	Denver, Colorado.
*Dr. H. E. Smith,	New Haven, Connecticut.
Dr. R. Meade Smith,	Colorado Springs, Colorado.
*Dr. G. M. Sternberg, Surgeon General, U. S. A.,	Washington, D. C.
Dr. G. N. Stewart,	Cleveland, Ohio.
Dr. W. G. Thompson,	New York City.
Dr. V. C. Vaughan,	Ann Arbor, Michigan.
*Dr. J. W. Warren,	Bryn Mawr, Pennsylvania.
*Dr. Wm. H. Welch,	Baltimore, Maryland.
Dr. W. P. Wilson,	Philadelphia, Pennsylvania.
*Dr. H. C. Wood,	Philadelphia, Pennsylvania.

ASSOCIATION OF AMERICAN ANATOMISTS.

Organized, September 17th, 1888.

ACTIVE MEMBERS.

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Dr. Edward P. Allis, Jr.,	Milwaukee, Wisconsin.
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Dr. E. A. Balloch,	Washington, D. C.
*Dr. A. D. Bevan,	Chicago, Illinois.
Dr. H. S. Birkett,	Montreal, Canada.
Dr. V. P. Blair,	St. Louis, Missouri.

*Dr. Joseph A. Blake,	New York City.
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Dr. N. E. Brill,	New York City.
Dr. F. J. Brockway,	New York City.
Dr. W. Allen Brooks, Jr.,	Boston, Massachusetts.
*Dr. Wm. Browning,	Brooklyn, New York.
Dr. Joseph D. Bryant,	New York City.
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Dr. C. E. Cotton,	Cleveland, Ohio.
Dr. J. D. Craig,	Albany, New York.
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*Dr. R. H. M. Dawbarn,	New York City.
Dr. John B. Deaver,	Philadelphia, Pennsylvania.
Dr. F. X. Dercum,	Philadelphia, Pennsylvania.
Dr. Franklin Dexter,	Boston, Massachusetts.
Dr. John M. Dodson,	Chicago, Illinois.
Dr. J. T. Duncan,	Toronto, Canada.
Dr. Thomas Dwight,	Boston, Massachusetts.
Dr. Robert G. Eccles,	Brooklyn, New York.
Dr. Harry B. Ferris,	New Haven, Connecticut.
Prof. P. A. Fish,	Ithaca, New York.
Dr. Thomas Flavin,	Galveston, Texas.
Dr. Wm. S. Forbes,	Philadelphia, Pennsylvania.
Dr. J. P. C. Foster,	New Haven, Connecticut.
Dr. Gilman DuBois Frost,	Hanover, New Hampshire.
Dr. Frank R. Fry,	St. Louis, Missouri.
Prof. Simon Henry Gage,	Ithaca, New York.
Dr. Bern B. Gallaudet,	New York City.
*Dr. Fred. Henry Gerrish,	Portland, Maine.
*Dr. Theo. Nicholas Gill,	Washington, D. C.
Dr. George Lincoln Goodale,	Cambridge, Massachusetts.
Dr. R. L. Greene,	Kansas City, Missouri.
Dr. Elisha H. Gregory, Jr.,	St. Louis, Missouri.
*Dr. Carl A. Hamann,	Cleveland, Ohio.
Dr. Isaac B. Hamilton,	Los Angeles, California.
Dr. Irving S. Haynes,	New York City.
Dr. C. J. Herrick,	Granville, Ohio.
*Dr. Addinell Hewson,	Philadelphia, Pennsylvania.
*Dr. E. R. Hodge,	Washington, D. C.
Dr. E. W. Holmes,	Philadelphia, Pennsylvania.
*Dr. Presley C. Hunt,	Washington, D. C.
*Dr. George S. Huntington,	New York City.
*Dr. Woods Hutchinson,	Buffalo, New York.
Dr. Horace Jayne,	Philadelphia, Pennsylvania.
Dr. Wm. Keiller,	Galveston, Texas.
*Dr. George T. Kemp,	Baltimore, Maryland.
*Dr. D. S. Lamb,	Washington, D. C.

Dr. F. W. Langdon,	Cincinnati, Ohio.
Dr. Thomas G. Lee,	Minneapolis, Minnesota.
Dr. Joseph Leidy,	Philadelphia, Pennsylvania.
Dr. Wm. Evan Lewis,	Cincinnati, Ohio.
Dr. John Lindsay,	Philadelphia, Pennsylvania.
Dr. F. A. Lucas,	Washington, D. C.
Dr. George McClellan,	Philadelphia, Pennsylvania.
Dr. Peter J. McCourt,	New York City.
Prof. O. C. Marsh,	New Haven, Connecticut.
Dr. Rudolph Matas,	New Orleans, Louisiana.
Dr. W. P. Mathews,	Manchester, Virginia.
Dr. Washington Matthews, U. S. A.	Washington, D. C.
*Dr. J. Ewing Mears,	Philadelphia, Pennsylvania.
*Dr. C. M. Miller,	Richmond, Virginia.
Dr. Chas. S. Minot,	Boston, Massachusetts.
*Dr. S. J. Mixter,	Boston, Massachusetts.
Dr. M. B. Moody,	New Haven, Connecticut.
Dr. R. O. Moody,	New Haven, Connecticut.
Dr. John T. Moore,	Galveston, Texas.
*Dr. J. F. Moran,	Washington, D. C.
Dr. J. D. Morgan,	Washington, D. C.
Dr. J. C. Munro,	Boston, Massachusetts.
Prof. H. F. Osborn,	New York City.
*Dr. Clayton Parkhill,	Denver, Colorado.
Dr. John Parmenter,	Buffalo, New York.
Dr. George A. Piersol,	Philadelphia, Pennsylvania.
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Dr. Robert Reyburn,	Washington, D. C.
*Dr. John B. Roberts,	Philadelphia, Pennsylvania.
Dr. A. L. T. Schaper,	Boston, Massachusetts.
Dr. Wm. B. Scott,	Princeton, New Jersey.
*Dr. F. J. Shepherd,	Montreal, Canada.
Dr. R. W. Shufeldt,	Washington, D. C.
Dr. D. K. Shute,	Washington, D. C.
Dr. Chas Dennison Smith,	Portland, Maine.
Dr. Eugene A. Smith,	Buffalo, New York.
Dr. Edmond Souchon,	New Orleans, Louisiana.
Dr. E. C. Spitzka,	New York City
Dr. Geo. D. Stewart,	New York City
Dr. Wm. O. Stillman,	Albany, New York.
Dr. Thos. B. Stowell,	Potsdam, New York.
Dr. B. B. Stroud,	Ithaca, New York.
Dr. Joseph P. Tunis,	Philadelphia, Pennsylvania.
Dr. P. Y. Tupper,	St. Louis, Missouri.
Dr. C. H. Ward,	Rochester, New York.
Dr. Faneuil D. Weisse,	New York City.
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*Dr. Burt G. Wilder,	Ithaca, New York.
Dr. Wm. P. Wilson,	Philadelphia, Pennsylvania.

Dr. Wm. C. Woodward,	Washington, D. C.
Dr. George Woolsey,	New York City.

HONORARY MEMBERS.

Mr. Wm. Anderson, F.R.C.S., etc.,	London, England.
Mr. Daniel John Cunningham, M.D., D.S.C., LL.D.,	Dublin, Ireland.
Sir Wm. Henry Flower, K.C.B., etc.,	London, England.
Mr. Wm. Turner, F.R.C.S., Ed., etc.,	Edinburgh, Scotland.

AMERICAN PEDIATRIC SOCIETY.

Organized September 18th, 1888.

ACTIVE MEMBERS.

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*Dr. S. S. Adams,	Washington, D. C.
Dr. Allen Baines,	Toronto, Canada.
Dr. A. D. Blackader,	Montreal, Canada.
*Dr. Wm. D. Booker,	Baltimore, Maryland.
*Dr. Dillon Brown,	New York City.
Dr. E. M. Buckingham,	Boston, Massachusetts.
Dr. Augustus Caillé,	New York City.
*Dr. Walter Lester Carr,	New York City.
*Dr. H. D. Chapin,	New York City.
Dr. W. S. Christopher,	Chicago, Illinois.
Dr. Frank S. Churchill,	Chicago, Illinois.
*Dr. Floyd M. Crandall,	New York City.
*Dr. Edward P. Davis,	Philadelphia, Pennsylvania.
Dr. John Dorning,	New York City.
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*Dr. J. Henry Fruitnight,	New York City.
Dr. E. E. Graham,	Philadelphia, Pennsylvania.
*Dr. J. P. Crozer-Griffith,	Philadelphia, Pennsylvania.
*Dr. L. Emmet Holt,	New York City.
Dr. F. Huber,	New York City.
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*Dr. A. Jacobi,	New York City.
*Dr. Chas. G. Jennings,	Detroit, Michigan.
*Dr. Charles J. Kerley,	New York City.
*Dr. Henry Koplik,	New York City.
*Dr. Henri Lafleur,	Montreal, Canada.
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*Dr. F. Gordon Morrill,	Boston, Massachusetts.
Dr. J. Lovett Morse,	Boston, Massachusetts.

*Dr. J. H. Musser,	Philadelphia, Pennsylvania.
*Dr. Wm. P. Northrup,	New York City.
*Dr. Joseph O'Dwyer,	New York City.
*Dr. Wm. Osler,	Baltimore, Maryland.
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*Dr. T. M. Rotch,	Boston, Massachusetts.
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Dr. A. Seibert,	New York City.
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*Dr. Louis Starr,	Philadelphia, Pennsylvania.
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Dr. V. C. Vaughan,	Ann Arbor, Michigan.
*Dr. Wm. Perry Watson,	Jersey City, New Jersey.
Dr. A. H. Wentworth,	Boston, Massachusetts.
Dr. James P. West,	Bellaire, Ohio.
Dr. T. S. Westcott,	Philadelphia, Pennsylvania.
Dr. Harold Williams,	Boston, Massachusetts.
*Dr. James C. Wilson,	Philadelphia, Pennsylvania.
Dr. Joseph E. Winters,	New York City.
*Dr. Leroy M. Yale,	New York City.

The following were present as

VISITORS

to various of the component Associations.

Colonel C. H. Alden, U. S. A.,	Washington, D. C.
Dr. C. L. Allen,	Washington, D. C.
Dr. C. P. Ambler,	Asheville, North Carolina.
Dr. A. R. Amos,	Des Moines, Iowa.
Dr. Helen G. Baldwin,	Philadelphia, Pennsylvania.
Dr. L. Blake Baldwin,	Chicago, Illinois.
Dr. Newton L. Bates, U. S. N.,	Washington, D. C.
Dr. E. Oliver Belt,	Washington, D. C.
Dr. John A. Blair,	New Castle, Pennsylvania.
Dr. J. Bion Bogart,	Brooklyn, New York.
Dr. S. G. Bonney,	Denver, Colorado.
Dr. W. S. Bowen,	Washington, D. C.
Dr. J. R. Bromwell,	Washington, D. C.
Dr. Sanger Brown,	Chicago, Illinois.
Dr. James Burry,	Chicago, Illinois.
Dr. J. Payson Clark,	Boston, Massachusetts.
Dr. Wm. B. Coley,	New York City.
Dr. C. C. Fite,	New York City.
Dr. Robert Fletcher,	Washington, D. C.
Dr. Wm. H. Fox,	Washington, D. C.
Dr. L. F. French,	Washington, D. C.

Dr. T. H. Halsted,	Syracuse, New York,
Dr. T. V. Hammond,	Washington, D. C.
Dr. Ida J. Heiberger,	Washington, D. C.
Dr. George T. Howland,	Washington, D. C.
Dr. Gordon King,	New Orleans, Louisiana.
Dr. A. H. Knapp,	New York City.
Dr. S. A. Knopf,	New York City.
Dr. John L. Leal,	Paterson, New Jersey.
Dr. Daniel Lewis,	New York City.
Dr. John J. H. Love,	Montclair, New Jersey.
Dr. James F. McKennan,	New York City.
Dr. A. F. Magruder, U. S. N.,	Washington, D. C.
Dr. G. L. Magruder,	Washington, D. C.
Dr. E. B. Mathiot,	Pittsburgh, Pennsylvania.
Dr. C. S. Millet,	Brockton, Massachusetts.
Dr. W. B. Moulton,	Portland, Maine.
Dr. S. B. Muncaster,	Washington, D. C.
Dr. John H. Mundell,	Washington, D. C.
Dr. Wm. M. Nagle,	Denison, Texas.
Dr. O. T. Osborne,	New Haven, Connecticut.
Dr. T. C. Phillips,	Milwaukee, Wisconsin.
Dr. Ira J. Prouty,	Keene, New Hampshire.
Dr. W. A. Pusey,	Chicago, Illinois.
Dr. C. W. Richardson,	Washington, D. C.
Dr. P. M. Rixey,	Washington, D. C.
Dr. H. A. Robbins,	Washington, D. C.
Dr. A. Schloss,	Stockton, California.
Dr. T. S. Southworth,	New York City.
Dr. Z. T. Sowers,	Washington, D. C.
Dr. T. L. Stedman,	New York City.
Dr. John Stewart,	Halifax, Nova Scotia.
Dr. I. S. Stone,	Washington, D. C.
Dr. J. E. Stubbert,	Liberty, New York.
Dr. R. T. Taylor,	Baltimore, Maryland.
Dr. Jacob Teschner,	New York City.
Dr. F. C. Thayer,	Waterville, Maine.
Dr. Max Thorner,	Cincinnati, Ohio.
Dr. H. S. Walrath,	St. Paul, Minnesota.
Dr. J. K. Weaver,	Norristown, Pennsylvania.
Dr. J. P. West,	Bellaire, Ohio.
Dr. B. T. Whitmore,	Chicago, Illinois.
Dr. E. L. Williamson,	New York City.
Dr. Charles Wirgman,	Philadelphia, Pennsylvania.
Dr. H. C. Yarrow,	Washington, D. C.

RECAPITULATION.

	Members.			
	Active	Honorary.	Corresponding.	Present.
American Ophthalmological Society.	136	1	..	58
American Otological Society	97	5	..	34
American Neurological Association..	90	7	14	49
American Gynecological Society....	90	28	..	58
American Dermatological Association	40	8	..	26
American Laryngological Association	69	1	22	40
American Surgical Association.....	89	22	..	58
American Climatological Association	122	3	..	49
Association of American Physicians..	100	7	..	67
American Association of Genito-Urinary Surgeons.....	48	..	..	22
American Orthopedic Association....	51	8	20	28
American Physiological Society.....	62	..	..	25
Association of American Anatomists.	108	4	..	25
American Pediatric Society.....	54	..	..	31
	1156	94	56	570
Total Members of Congress.....	...	..	..	1306
Guests and Visitors.....	...	..	..	65
Total in attendance.....	...	..	..	635

THE GOUTY AND RHEUMATIC DIATHESIS WITH RELATION TO DISEASES OF THE EYE.

Lesions in the Retinal Vessels, Retina and Optic Nerve, Associated with Gout.

BY CHARLES STEDMAN BULL, A.M., M.D. (COLUMBIA).

Professor of Ophthalmology in the University of the City of New York.

At the meeting of the American Ophthalmological Society held in 1893, the writer presented a paper on Gouty Retinitis and Neuro-Retinitis, in which he gave a somewhat detailed résumé of our existing knowledge of the changes produced in the vascular system by the influence of the gouty diathesis. For a full account of these changes and of the investigations of various observers in this direction, the writer would refer to the above paper, published in the Transactions of the American Ophthalmological Society for that year.

In the four years which have elapsed since the paper was published, the conclusions which the writer then reached have been strengthened, and he can speak still more positively of the changes in the retina and optic nerve, and in the retinal vessels, which are not infrequently met with in gouty patients.

The pathological condition of the blood in gout does not always work in a way that readily attracts attention, and this is particularly true in regard to the eye.

Most authors who refer to retinal complications occurring in the course of gout, mention only a hemorrhagic retinitis as being the most frequent retinal complication.

I do not think that there is any doubt as to the existence of a gouty retinitis or neuro-retinitis, which strongly resembles certain types of syphilitic retinitis, and which may or may not be accompanied by retinal hemorrhages and opacities in the vitreous humor.

The occurrence of the retinal hemorrhages is easily explained, for it is well known that gouty persons are prone to hemorrhages, venous obstruction, and irregularities in circulation, due to a great arterial pressure and a relaxed condition of the vascular walls, and vitreous opacities may in these cases be present. These hemorrhages may involve one or both eyes, and are of sudden onset.

Small linear and flame-shaped extravasations of blood may be strewn all over the fundus. At the same time the optic discs may be hazy and the retinal veins engorged and tortuous.

The effects of the poison of gout upon the vascular system are: a high blood-pressure in the arteries; hypertrophy of the left ventricle, and hard, incompressible arteries undergoing atheromatous degeneration. The influence of gout in the development of arterio-sclerosis and endarteritis is now well established. Arterial degeneration is hereditary in certain gouty families, and signs of arterio-sclerosis are very often the first symptoms of the hereditary malady.

Most of our knowledge of this condition of the arteries has been gained from Thoma's investigations, and we now recognize that arterio-sclerosis is caused by some general disturbances of nutrition, which are partly the result of infection, intoxication and other pathological lesions as yet but little understood, and partly the accompaniment of senile changes. We learn from Thoma that gout may be looked upon as the remote antecedent of endarteritis, and that the latter condition is by no means always reached through the medium of interstitial nephritis.

Changes in the constitution of the blood-current, such as are met with in gouty patients, would be very likely, in fact almost certain, to develop obstructive circulation in the capillary system. This condition of the capillary circulation must cause some change in the blood-current in the arteries. Whenever the blood-current is slow, the middle coat of the artery contracts; and when the latter does not occur, a new growth of connective tissue is developed in the tunica intima, which thus reduces the arterial calibre. The muscular coat of the artery first becomes involved, and the loss of elasticity permits the artery to dilate. As a result the blood-current becomes slow and in consequence the vaso vasorum becomes distended, and a new growth appears in the intima, and is followed by the same process in the other coats.

A similar condition is met with in the veins, and in fact the phlebo-sclerosis or endo-phlebitis may precede the endarteritis sometimes by a lengthy period.

Both these conditions, endarteritis and endo-phlebitis, are found much more frequently in the retina of persons who suffer from the chronic, non-inflammatory, atypical gout, than in those attacked by the typical inflammatory form of the disease, and the same thing is asserted to be true of the interstitial nephritis.

One of the results of this retinal endo-phlebitis is œdema of the

retina, which is one of the constant symptoms in the early stages of the disease. The circulation may become re-established through the obstructed vessels, in which case this œdema disappears; but if the obstruction to the blood-current becomes permanent, the distant venous branches become dilated and in places varicose. The hemorrhages which are met with are due to local softening of the vascular wall, or to the rupture of these minute varicose dilatations. They may be all shapes and sizes, small and punctate, linear or flame-shape, and scattered all over the fundus.

The scope of this paper is limited and is confined to a consideration of the changes in the retinal circulation in the retina itself, and in the optic nerve, as seen with the ophthalmoscope. The literature on the subject is very scanty. None of the older authors make any mention of retinal complications in gout, and until very recently nothing has been said or written of any changes in the retinal vessels.

Gauté (Thèse de Paris, 1881) speaks of a gouty retinitis resembling syphilitic retinitis, which may or may not be accompanied by opacities of the vitreous and retinal hemorrhages.

Lychon (Thèse de Paris, 1885) mentions neuro-retinitis and intraocular hemorrhages as being due to gout.

Nettleship (Diseases of the Eye, 4th Ed., 1890) says: "Hemorrhagic retinitis is more commonly met with in gouty persons than in others. It may be unilateral or bilateral. The children or descendants of gouty persons, without being themselves subject to gout, are liable in early life to this insidious form of eye disease."

This opinion had been previously stated by Jonathan Hutchinson, who has since again confirmed it.

Gowers (Medical Ophthalmoscopy, 1890) speaks more positively in regard to retinal lesions in gout. He thinks that the characteristics of these causes are: the greater degree of disturbance of vision than corresponds to the visible changes in the fundus, the tendency to irregular defects in the field of vision, and the presence of lesions of the retina and optic nerve of the other eye, induced by a symmetrical morbid process.

Galezowski (Annali di Ottalmologia, XIX) believes that the changes begin in the retina and extend to the choroid, giving rise to a retino-choroiditis, characterized by an alteration in the vessels and deposits in and outside their walls. All around the macula and along the vessels are brilliant patches of exudation. The inflammatory process occupies the central zone of the fundus, develops

slowly, usually involves both eyes, and never ends in total blindness, as the periphery of the retina is rarely affected.

In the Bericht der 25ten Versammlung der Ophthalmologischen Gesellschaft: Heidelberg, 1896, Wagenmann has a very interesting article on Eye Diseases in Gout, in which he admits that the diagnosis is not always easy in cases of atypical gout. After a careful study of the subject, he is convinced that the blood-current containing an excess of water irritates and inflames the tissues; or else that the uric acid and other products of animal combustion are extravasated in minute quantities in the tissues. The inflammatory process may be so marked that relatively large deposits appear in the tissues. The origin of these deposits in the eye is best explained by the Ebstein theory, according to which the blood with excess of urates sets up an inflammatory process in places where the circulation is slow. The well known changes are sero-plastic inflammation and a deposit of what Wagenmann calls "concrements." This is undoubtedly the cause of the patches of exudation, the numerous small hemorrhages, the narrow arteries and the marked venous hyperæmia seen in the retina, and also of the recurrent vitreous opacities, which are often of a distinctly hemorrhagic character.

In the discussion which followed the reading of Wagenmann's paper, Nieden, in agreeing with the author of the paper, stated that he regarded the recurring retinal and vitreous hemorrhages as almost pathognomic of gout.

Pflueger and Hirschberg also endorsed the views entertained by Wagenmann, and the latter called special attention to the presence of glistening inorganic deposits in circumscribed patches irregularly arranged around the macula lutea in gouty patients.

In my paper previously referred to, there was given the detailed clinical history of five cases and the reports of two autopsies, with the results of the microscopical examination of the retina and optic nerves. In the four years which have elapsed since that time, I have added to my data on the subject the histories of ten other cases, with the report of one autopsy.

The lesions to which I wish to call the attention of the Congress are:

1st. The changes in the walls of the blood vessels of the retina, choroid and optic nerve, including arteries, capillaries, and veins.

2d. Retinitis of a peculiarly localized character, confined to the posterior zone of the fundus, with or without hemorrhages in the retina and vitreous, and characterized by a peculiar yellowish exudation, occurring in clearly defined patches.

3d. Optic neuritis, generally with but sometimes without an accompanying retinitis.

The clinical history of the ten additional cases, on which this paper is based, resembles very closely that of the five original cases reported in the first paper, and the main facts are briefly repeated here.

The subjective symptoms consist in a deterioration of the vision, at first for small-size type, but later for all objects at any distance, and a certain degree of photophobia, most marked for artificial light. The ophthalmoscope shows more or less marked blurring of the outlines of the optic discs, resembling the first stage of papillitis, but without the œdematous swelling. The retinal arteries are diminished in calibre, in some places the lumen being reduced to the merest thread, and requiring the closest examination to see the minute blood column that still exists.

The white lines along the vessels, both arteries and veins, are broad and distinct, and extend from the centre of the papilla well out towards the periphery of the fundus. Occasionally the veins in places seem dilated like a fusiform aneurism, the vessel on both sides of the dilatation being reduced in calibre.

Yellowish-white patches of exudation, at first brilliant, but subsequently becoming dull, of varying size and shape, are seen mainly grouped about the region of the macula and disc, but with no systematic arrangement. These patches of exudation are entirely in the inner layers of the retina, as proved by the microscope. If hemorrhages are present, they are linear or flame-shaped in character, occur close to the vessels, both arteries and veins, and while mainly grouped around the posterior pole of the eye, are sometimes found scattered all over the fundus.

If opacities of the vitreous are present, they are the floating variety, are of small and of varying shape, and may be either the result of previous hemorrhages, or an evidence of coexisting choroiditis.

The ophthalmoscopic pictures in these cases is that of general retinal angio-sclerosis, with the addition of the glistening patches of exudation in the retina.

These patients had all shown signs of extensive degeneration of the walls of the blood vessels throughout the body, notably in the temporal and radial arteries.

The urine of these patients was usually of moderately high specific gravity, ranging from 1020 to 1026. It was loaded with uric acid

and phosphatic acid crystals. I have occasionally found a little albumen, but never any sugar or casts.

Of the five cases previously reported, two had died previous to the presentation of the first paper, and the results of the two autopsies have been published. Since then cases II and III have died, both of cerebral hemorrhage. Case I is still living and possesses enough vision to assist him in going about.

Of the ten cases seen since the presentation of the first paper, three have died: one from pneumonia and two from cerebral hemorrhage. I was fortunately able to secure an autopsy in one of the latter, and was permitted to remove the posterior parts of the eyeballs and the optic nerves for inspection. The results of the microscopical examination were almost identical with those of the two cases previously reported.

Sections made of the retina, choroid and optic nerve showed very extensive angio-sclerosis. The adventitia and media were decidedly thickened, but the main increase was in the intima, which in many cases was so marked as almost to obliterate the lumen. The proliferation in the adventitia was largely granular, while the thickening in the intima was mainly due to hyaline deposit. Numerous fusiform aneurysmal dilatations were found in the arteries, almost always at the point of origin of a branch, and on the distal side of these dilatations the calibre of the vessel was markedly narrowed. There were a number of hemorrhages, always close to the vessels. The nerve fibres on the papilla and in the retina were markedly varicose, and the spaces between them were filled by fine granular matter. In the retina the nerve fibre layer was thickened by infiltration of a mass of fine granules, aggregated in heaps, with occasional distinct cells filled with the same granular contents. These masses of fine granules extended through all the layers of the retina except that of the rods and cones, most of them however being in the nerve fibre layer. Sections of the optic nerve at various points as far back as the chiasm showed the same changes in the walls of the blood-vessels, and more or less marked varicosity of the nerve fibres, and small masses of fine granules.

The choroidal blood-vessels showed the same changes of angio-sclerosis. There were no patches of exudation found anywhere in the choroid, such as existed in the retina.

The following brief conclusions have been drawn from the cases presented.

1st. The changes in the fundus are always bilateral, though rarely

symmetrical in the two eyes. The lesion may begin simultaneously in the two eyes, but this is by no means always the case.

2d. The degenerative changes in the walls of the blood-vessels, both arteries and veins, are at first very minute and often overlooked. They must be carefully searched for, as they begin in the intima.

3d. The general angio-sclerosis and the patchy exudation in the retina cause marked impairment of central vision, but little impairment of peripheral vision, and the disease never ends in blindness.

4th. The loss of central vision is always progressive up to a certain point. Improvement of the vision, after the retinal disease is established, cannot be expected, though in favorable cases the existing vision may be maintained.

5th. Hemorrhages into the retina are rare except in the comparatively early stages of the disease. When the vessels lose their elasticity by reason of the increase in the thickness of their walls, due to the deposits, the vessels become stronger and more rigid, and hemorrhages are no longer to be feared.

6th. The most marked feature in the opthalmoscopic picture is the development of the angio-sclerosis in the vessels of the retina. This condition is confirmed by the microscope, and is seen to extend to the vessels of the optic nerve and choroid.

7th. Another almost equally marked symptom is the peculiar yellowish granular exudation in the retina, located by the ophthalmoscope around the posterior pole of the eye, and generally leaving the macula intact until late in the course of the disease. This exudation is shown by the microscope to be mainly in the nerve-fibre layer, though found in all the layers except that of the rods and cones.

8th. The changes in the optic nerves seem generally to be intra-ocular, but have been traced occasionally for some distance back of the eyeball.

THE GOUTY AND RHEUMATIC DIATHESES WITH RELATION TO DISEASES OF THE EYE.

Cataract and its Association with the Gouty and Rheumatic Diatheses.

BY S. D. RISLEY, M.D.

Attending Surgeon Wills' Eye Hospital, Philadelphia: Professor of Diseases of the Eye, Philadelphia Polyclinic and College for Graduates in Medicine.

It is not difficult to trace a distinct clinical relationship between a large group of ocular affections and the lithic acid diathesis. The eye symptoms from which many persons suffer disappear promptly under out-of-door life with the attending muscular exertion, deeper breathing and increased excretion. The blood vessels and tissues are relieved by these means of the products of imperfect metabolism consequent upon sedentary life, and the over-supply of rich foods. As a result, not only does the general health improve but the eye-symptoms disappear. While the relation of these ocular discomforts to the milder or incipient forms of lithæmia are too frequently overlooked, I believe it is quite as common to neglect the important bearing this diathesis has upon the more serious affections of the eye which occur especially during and after middle life.

The diseases of the heart and general vascular tree, the renal and hepatic complications associated with and in some sense dependent upon impairment of the ultimate processes of nutrition, the high arterial tension, the hypertrophied left ventricle, the chronic nephritis and contracted kidney, the rigid arterial walls becoming astheromatous, angina, apoplexies:—present a picture of serious disease which we are only too frequently called upon to witness.

It is not to be supposed that under these conditions the ocular blood-vessels can escape the disaster which has fallen so heavily upon the general vascular system, or that the eye alone should escape the general impairment of the nutritive functions. Indeed, when we consider that the nutrient membrana of the eye,—the choroid, is a meshwork of blood vessels, ramifying through a loose connective tissue stroma, we are prepared *a priori* to expect the striking clinical picture of disease so frequently presented to the ophthalmic surgeon for study. Indeed, he enjoys by the aid of the magnified ophthalmoscopic image, a unique opportunity to study pathological change progressing in living structures.

It is under these peculiarly favorable conditions that he is permitted to study the steadily-advancing degeneration of the retinal blood-vessels, i. e., the arterio- and phlebo-sclerosis; the formation of yellowish-white spots or splotches of exudation in the region of the macula or between the macula and optic nerve, or possibly distributed more widely over the eye ground; or, to witness the innumerable small retinal apoplexies in so-called hemorrhagic retinitis, in the later stages of nephritis, in perivasculitis and hemorrhagic glaucoma; and also the choroidal disease which so uniformly precedes incipient cataract, and upon which, it is the contention of this thesis, the cataract in large measure depends. In all of these diseases in a considerable number of cases the blood-vessel change which has so seriously disturbed the nutrition of the eye, has for months, or it may be for years, been steadily advancing *pari passu*, with corresponding changes going on in the general vascular system. The grave forms of eye disease which have been enumerated always lead the thoughtful physician to a careful and painstaking analysis of general conditions, and they usually prove to be but one of many other groups of symptoms pointing to general impairment of the vital functions. It is this fact which makes these forms of ocular disease with hemorrhage so ominous of cerebral apoplexy.

The frequent occurrence of cataract in association with the grave forms of general and local disease which have been mentioned, and the fact that like these it appears during and after middle life, when the stress of living has begun to wear upon the complex organism, suggests a probable relation of cause and effect.

The classification of hard cataract as *senile* has, however, served in great measure to fix attention upon the age of the patient as the principal etiological factor, and to obscure its possible relations to local and general pathological states which in their essential nature are very far removed from the evidences of physiological decline which are characteristic of a normal and peaceful old age.

It should be borne in mind that, while the lens loses its elasticity and becomes hard or even straw-colored as age advances, and by this manifests its participation in those inevitable changes quite correctly regarded as senile, it, nevertheless, is only in exceptional instances that it loses its transparency to a degree which seriously impairs the acuity of vision. It is, moreover, true that in many persons of great age, and in others where the signs of senility are exceptionally pronounced, the transparency of the lens is preserved to the last, as is demonstrated by their excellent sharpness of vision. When

therefore the lens undergoes not only physiological hardening, but becomes also opaque, it should suggest the presence of pathologic causes for this extraordinary occurrence.

It is unquestionably true that opacity of the lens frequently occurs where we can discover no trace of the rheumatic or gouty diathesis in the individual or his ancestry, but I have been at pains to show that even in these individuals the incipient cataract was so uniformly preceded by retino-choroidal disease and vitreous degeneration as to enforce the opinion that the opacity of the lens was a result of impaired nutrition caused by the associated affections of the uveal tract.* In sixty consecutive cases of incipient cataract between 42 and 82 years of age, occurring in private practice, it was shown that in upward of 50% there was noted a clear history of weak eyes and long-standing asthenopia, often reaching back into early life. Choroiditis in varying degrees of severity, with vitreous opacities, is noted and in most instances carefully described in one or both eyes in 60% of the cases. In the remaining 40% no note is made of the intra-ocular conditions or the opacity was too far advanced to permit ophthalmoscopic study of the fundus, but in many of these the intra-ocular disease was rendered probable by the weak and irritable eyes, asthenopia, and the chronically injected or inflamed extra-ocular membranes. That is to say, there was present undue sensitiveness to light, headache and increased lachrymation. The conjunctiva of the lids was injected, the caruncles swollen and red, while the episcleral and anterior perforating vessels were full and tortuous, indicating unmistakably the pathological processes progressing within the eyeball.

In a word, in these sixty cases of incipient cataract applying consecutively for relief and presenting all stages of advancement in one or both eyes, there could be no doubt as to the relation of cause and effect between the advancing opacity of the lens and the attending pathological conditions of the uvea. This view was furthermore confirmed by the fact that in many of these patients no sooner had the opacity sufficiently advanced to exclude the light from the eye and thus prohibit its use, than the external irritation and asthenopia more or less rapidly subsided.

That the lens and vitreous body should undergo degenerative changes in an eye, the subject of pathological processes affecting its food-bearing membrane, should not cause surprise, since it should be

* "Incipient Cataract: Its Etiology, Prognosis and Treatment." By S. D. Risley, University Med. Mag., March, 1889.

anticipated that these avascular structures would quite naturally be the first to suffer from impaired nutrition. We are accustomed to witness opacity of the lens as a sequel to violent forms of disease involving the uveal tract, as in plastic irido-cyclitis, detachment of the retina and absolute glaucoma, in all of which it is very liable to occur as the closing scene in these destructive processes.

That less vicious forms of uveal disease may also be influential in leading to impairment of the nutrition of the lens and causing it to become opaque, and that the gouty rheumatic diatheses are among the most frequent causes of these chronic sub-acute forms of disease affecting the uvea, is the contention of this paper. I suppose that no one will be found to question the clinical fact that these important dyscrasiæ are second only to syphilis in causing iritis and irido-cyclitis, especially in their recurrent forms. But any careful study of individual cases will reveal the fact that the entire choroidal tract is also more or less seriously involved in every case. Indeed, it not infrequently happens that the acute recurrences of iritis are preceded by a lighting up of the deeper chronic and progressive choroiditis under exacerbations of the rheumatic or gouty diathesis. That many of these exacerbations never result in iritis, but are manifested by asthenopia, slightly increased impairment of vision, and tender eyeballs is doubtless true, but each attack disturbing more and more profoundly the nutrition of the eyeball. Such attacks are often attended with transient increase of tension, a steamy cornea, and foggy, vitreous body. When examined with a magnifying glass this want of transparency in the vitreous is seen to be due to a fine granular or sand-like deposit which clears up as the attack passes off. Under repeated exacerbations web-like opacities finally form which float more and more freely as the vitreous degenerates and loses its normal consistency. The nucleus of the lens becomes more and more plainly outlined and the lens substance more strongly reflecting. In many cases banks of opacity form in the periphery, from which spicules of opacity sooner or later project along the capsule towards the pole.

The following case, in which the cataract was but one of the phenomena in a long chain of symptoms depending upon the diathesis under discussion, will serve to illustrate the group of cases I have in mind. Mrs. S., aged 62, consulted me in 1884, complaining of recurring attacks of headache, during which she was unable to use her eyes. During these attacks the eyeballs were tender to palpation, there was increased lachrymation and undue sensibility to

light. Retiring at night in her usual health, she would rise in the morning with an exacerbation of her ocular disturbance and headache, which was frequently attended with tinnitus, impaired hearing and foggy vision, the latter often so marked as to make reading not only painful but difficult. At her first visit V.=6—vii½ with glasses which corrected a low grade of hypometropic astigmatism. The pupils dilated medium only, under homatropine. The lenses were strongly reflecting and a few opaque spicules were present in the lower and inner periphery of each. The retinal arteries were small and had gray borders near the optic nerve. The veins were relatively large and dark with gray edges in places, and in others granular borders. The choroid was honeycombed, while yellowish spots and blotches were distributed throughout the eye ground, but were larger and more numerous in the region of the macula, and between it and the temporal border of the nerve. The details of the fundus were slightly blurred, but careful study with +8. behind the ophthalmoscopic mirror showed the anterior part of the vitreous filled with a fine sand-like deposit.

She became short of breath on exertion, and observed that this had slowly increased during the past year or two. There were no heart murmurs, but she had a high tension pulse and rigid but not stiff radial arteries. The specific gravity of the urine was 1028, and was loaded with uric acid, which crystallized on standing, but no albumen or sugar was present. She was subject to frequently recurring redness and tenderness of the joints and chalky concretions were forming in the fingers of both hands. There was a clear history of gout on the paternal side for three generations. I have watched the gradual advance of all these conditions since 1884. The sclera have become more rigid, the pupils now dilate but little under a mydriatic, the spicules in the lenses have slowly advanced in both anterior and posterior cortex, and the anterior capsule has become gray and streaked, with here and there grayish white spots of opacity apparently lying just beneath it. The nucleus of the lens is plainly outlined, and with a convex glass is granular in appearance. Opacities float freely in the vitreous with every movement of the eye, and vision has fallen to ⅕. To all appearance she is now the victim of rapidly maturing cataract. The present state has been reached by frequently occurring exacerbations of mild gouty attacks. Many times the eyes would escape, the attack falling upon the joints, but frequently the eyes alone would suffer, sometimes one, but often both at the same time.

The vision has often fallen below the usual average, and the vitreous would be found filled with a granular débris and web-like opacities which, under the local installation of homatropine and the administration of drugs internally, mild catharsis, baths and careful diet, would slowly clear up and vision rise to its usual standard. The vitreous opacities are large, and float with much greater freedom than formerly, a fact indicating the increased fluidity and disorganization of the vitreous.

In the meantime the radial arteries have become astheromatous, while the ability to take exercise has slowly diminished, until she has been compelled to seek a bedroom on the first floor to avoid ascending the stairs.

The failure of vision, consequent upon the opacity of the lens and vitreous, now makes it impossible to read, except large type. She has, in a word, arrived at the stage of cataract at which many of our patients first seek advice, but this patient was one of those who frequently sought relief from her eye and ear discomforts, so that I have had the unusual opportunity of tracing the steady course of her disease through many years. That her case presents an unusual history, however, I do not believe. I am led to this conclusion by the very frequent association of cataract with the other groups of symptoms characteristic of steadily advancing lithæmia. This frequent association is manifested by the careful search for general vascular disease, and renal affections made by the ophthalmic surgeon in every case of cataract, first applying for relief, before operation is advised. It is probably true that this is done rather in the interest of a careful prognosis than to establish any pathological relation between the disease in question and the occurrence of the cataract, but I am convinced that the opacity of the lens should be viewed as one of the protean manifestations of the general disease. Although it may not be possible to trace the degeneration of the lens fibres directly to the presence of uric acid or its salts in the nutrient fluids which surround it, it is highly probable that its nutrition suffers impairment through the disease of the membranes upon which it, in common with the other ocular tissues, depends for suitable pabulum.

That the nutrition of the lens should suffer in the presence of this diathesis is rendered at least probable by several considerations other than those already adduced. It is in the first place, to be expected that what may be termed the unstable equilibrium of the component transparent cells of the lens would be readily disturbed, as others have pointed out, by qualitative change in its environing

fluids. For example, it is well known that the entrance into the tissues of the frog of rapidly diffusible substances, as chlorid of sodium, naphthalin and sugar, disturb the transparency of the lens, presumably through some change in the normal osmotic qualities of the fluids in and around the lens. I have, in three instances, seen curious and interesting changes suddenly occur in the refraction of diabetic patients during acute exacerbations of their disease presumably due to changes in the lens, which once more resumes its normal state when the great excess of sugar had disappeared from the urine, and presumably also from the tissues.*

It is probable, having these observations in view, that the change in the density of the tissue fluids was sufficient to disturb the physiological relation of osmosis in the lens fibres, and thus lead to the observed changes in the refraction of the eye. If this can occur in saccharine diabetes, why may not a similar change be produced by the accumulation in the blood and fluids of the tissues of lithic acid and its salts? While the lens may recover from a single disturbance, as noted in the three cases of diabetes mentioned above, it is highly probable that permanent degeneration would ensue upon repeated exacerbations, or if the lens were steadily bathed in an abnormal nutritive fluid. The excess of uric acid salts in the serum in the rheumatic or gouty diathesis may be and doubtless is sufficient to disturb the nutritive equilibrium in all the organic cells, but would fall with especially disastrous results in the unstable transparent cells of the lens and vitreous body. The amount of uric acid in the gouty blood may, according to Gerrod, reach .11 grain in 1,000 grains of serum. Furthermore, the clinical fact as bearing upon the conclusion of this paper that the ectodermic structures of which the lens is one, and the connective tissue in and about the joints where it is the most dense and comparatively avascular, and therefore, where nutrition is most easily retarded, are precisely the localities which suffer earliest and most constantly in the evolution of gout.

That the existence of advanced atheroma adds to the risks of operation for cataract is unquestionably true. This was demonstrated in the case of an aged woman, already published, the subject of advanced atheroma, blind with over-ripe cataract in both eyes. The usual section was completed, but before the next step in the operation could be taken, she cried out with violent pain in the occiput. The lens was forcibly extruded from the wound and was

* Transactions of the American Ophthalmological Society, for 1897.

followed immediately by a profuse gush of a yellowish vitreous fluid, and this by a stream of bright red blood, so copious as to run over the face and saturate the pillow. The brittle intra-ocular blood vessels had ruptured under the removal of their usual support, afforded by the ocular tension, which was suddenly disturbed by opening the anterior chamber. The eye was of course lost, but what is of more significance in this discussion is the fact that a month later she became the victim of a fatal intra-cranial apoplexy.

THE GOUTY AND RHEUMATIC DIATHESES WITH RELATION TO DISEASES OF THE EYE.

Gout and Rheumatism as Factors in the Etiology of Glaucoma.

BY STEPHEN OLIN RICHEY, M.D.,
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Within the past year an eminent colleague said to me, "I think iridectomy in chronic glaucoma is indefensible; but what is glaucoma?" Agreeing with him, as I do, in regard to operation in chronic glaucoma, it is yet with some diffidence that I essay this consideration of the malady.

The least confusing presentation of the subject is under its two extreme forms, acute inflammatory glaucoma, and chronic simple glaucoma. All other varieties occur between these two, partaking more or less of the one or the other, due to the same cause, in differing degrees of intensity; including even so-called secondary glaucoma, which may be *secondary* to keratectasia, or fistula of the cornea, in which affections the support to the blood vessels of the fundus is diminished by the subnormal intra-ocular tension in the same way as by a mydriatic: to irido-cyclitis, or retinal hemorrhage, dependent upon gout: occlusion of the pupil, luxation of the lens, intra-ocular tumors, choriditis, myopia; any of them may cause the increase of tension of a pseudo-glaucoma, but not the intra-ocular tension characteristic of true glaucoma. Secondary glaucoma has a defined local exciting cause, but there is also a constitutional predisposition, as in glaucoma following cataract extraction.

Propositions.

First. Increased intra-ocular tension in glaucoma is caused chiefly by distension of the blood-vessels internal to the sclerotic; rarely, and to a slight degree, by derangement of intra-ocular secretion, or excretion.

Second. Associated with increased intra-ocular tension, is high general arterial tension, or arterio-sclerosis, pulsation of the intra-ocular arteries and veins, with probable hypertrophy, but at least functional disturbance, of the heart.

Third. As a result of persistent venous stasis, thrombosis and hyperplasia of connective tissue with substitution (substitutive fibrosis) takes place in all the tissues of the bulb.

Fourth. In chronic glaucoma the *materies peccans* of rheumatism cannot be excluded as a factor in causation: no reason appears for suspecting it of any agency in acute glaucoma.

Fifth. Every form of glaucoma is owing primarily to gout (or goutiness), or to acquired syphilis in its tertiary stage.

Sixth. Iridectomy, the first violence of the attack being past, so reduces intra-ocular pressure as to permit the vena vorticosae to be emptied, thus restoring the intra-ocular circulation and establishing normal tension. Any operation which lessens the surface pressure upon the vascular system within the eye, whatever the result, seems in reason open only to this explanation; for such vessels have no vaso-motor* system, and no power of contraction, but dilate and contract in response to the greater or less force of the extra-ocular blood current.

Intra-ocular tension in a normal eye is increased at every *pulse beat*†, and at every expiration; and is lessened during inspiration. By experiment, retardation of the venous outflow increases pressure in the vitreous, and lowers it in the aqueous chamber; the venous outflow being normal, a reduced arterial supply lowers tension, and *per contra;* showing the control of intra-ocular tension by the intra-ocular, depending upon the general, vascular condition. To the hypothesis of a derangement of the functions of secretion and excretion as a cause of high intra-ocular tension, serious, if not insuperable, objections exist, although it has been accepted for many years as the best offered. It is based upon an assumption that "increased intra-ocular tension is the essence of the disease" and the cause of all its evils, and that glaucoma is purely local. It is unsatisfactory to one who has watched an attack of acute glaucoma from its manifest inception, unless he be willing to ignore the constitutional history and complications of the malady; or to one

* Gray (Anatomy, 8th Edition, p. 77) quotes Kolliker, "The majority of the arteries of the brain and spinal cord, and *those of the choroid* are unprovided with vaso-motors."

Norris and Oliver, System of Diseases of the Eye, Vol. I, p. 261: "Since the nervous supply of the choroid is especially distributed to the muscular tissue of the blood-vessels, the component fibres *may be regarded* as vaso-motor in character."

(Physiology, Landois and Stirling, 2d Ed., p. 623), "According to Klein and Svetlein, the retinal vessels are not influenced by division, or stimulation, of the sympathetic."

† The dependence of intra-ocular tension upon the extra-ocular arterial tension is shown by some late "Observations on the Retinal Blood-Stream." (C. H. Usher, Oph. Rev., Dec. 1896.)

who has followed the progress of a chronic glaucoma through all its phases and modifications, not limiting his observation to the special local developments. The disease has been correctly defined as "a complex of symptoms," for the involvement of each component tissue of the bulb compels it to give voice to its distress. Though high intra-ocular tension is a cause of some of the other symptoms, derangement of intra-ocular secretion could not accomplish what we find in glaucoma. If there were at the same time increased secretion and retention, the intra-ocular contents, by the action of both, would only the more quickly reach a point short of the high tension of acute glaucoma at which the resistance to secretion would be too great for its continuance; for the secretion of aqueous is a transudation, an osmosis, and lacks the intensity even of a glandular secretion. The term *secretion* offers no conception of energy.

Such an objection would seem to be fatal to the theory, though it is not claimed that secretion is not increased, or retained, in glaucoma; only that by this means a higher degree of intra-ocular tension *cannot* be produced than is to be found in serous iritis. It is a mere question of physics. That glaucoma has occurred in cases of aphakia, of aniridia, and in others in which the anterior filtration channels were found patulous, would prove that impeded excretion had no agency in those instances. In view of such observations, when the anterior filtration channels are found closed by dissection of an eye after the disease had run its course, we are not justified in assuming that the disease was due to impeded excretion.

Again, periods of increased intra-ocular tension occur, and pass off without mechanical interference, as in the prodromata: could this be, if it were caused by closure of the anterior filtration channels?

The character of that obstruction is usually such, that once "the vicious circle" is formed, it can be broken only by foreign aid. Has the volume of the intra-ocular fluids (exclusive of the blood within the vessels) any important bearing upon the high intra-ocular tension of glaucoma?

Advancement of the lens and iris is ordinarily observed in glaucoma, with no apparent pathological changes in the vitreous; if the *volume* of the vitreous did vary, its consistency is such as to preclude the rapidity of variation necessary to account for the modifications of tension in the eye. An increased volume of aqueous humour in the eye cannot produce advancement of the lens and iris (much less of the corpus vitrei), it being in front of the lens, and able to

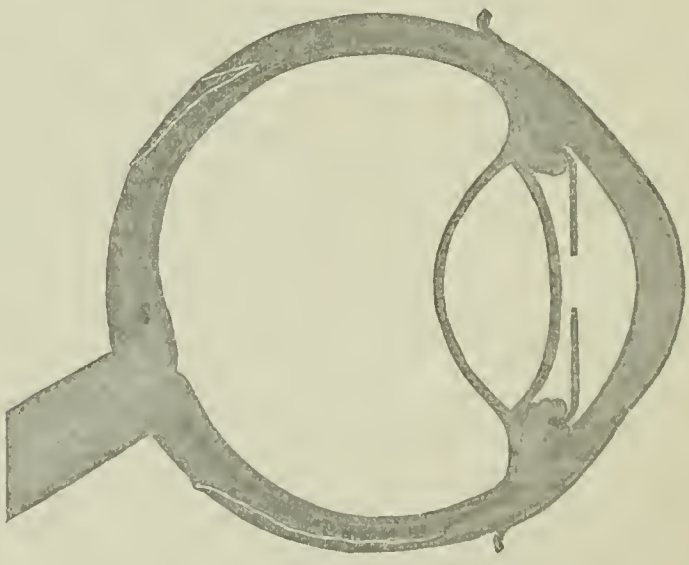
distribute itself easily and equally on both sides of the iris, without pressure upon it. If the anterior channels of filtration were obstructed, the impaired outflow in this direction would increase the depth of the anterior chamber, as in serous iritis. When occlusion of the pupil occurs in plastic iritis, and the aqueous humour secreted behind the iris forces it forward in contact with the cornea, we do not promptly have a glaucoma as a result. When the anterior filtration channels are closed by the iris, the lens and iris must *have* advanced, or the iris must *have been* dilated, by pressure from behind by a condition *already* present, which causes advancement of the vitreous, lens and iris, and increased intra-ocular tension. Also, when the aqueous is diminished by evacuation through a corneal incision, do not the lens and iris advance promptly to the posterior surface of the cornea? A normal volume of aqueous humour maintains a normal anterior chamber: an increased volume deepens, and a *reduced* volume of aqueous shoals the anterior chamber. Must not such an evacuation take place very slowly to avoid rupture of the distended blood vessels of the fundus by the sudden removal of the support in front to the *vis a tergo* of the general arterial pressure? It is an engorgement of the blood-vessels of the fundus depending upon the pressure in the extra-ocular arterial vessels, upon the force of a bounding heart, which, *after iridectomy*, causes intra-ocular hemorrhage in the case of rotten vessel coats; that in some instances prevents the restoration of the anterior chamber; that may end, if the general arterial pressure is sufficiently great and sustained, in malignant glaucoma.

The only rational explanation of a good result from iridectomy in glaucoma is, that a happy moment is chosen when the first force of the storm is spent, and the operation, by easing the pressure upon the intra-bulbar tissues and vessels, permits the static venous blood to move, and *active* circulation to be restored. This moment may be designedly secured, by first relieving general arterial tension and quieting the action of the heart by a heart-sedative; better, by *hot* baths. To operate under other circumstances may mean an untoward result, and probably accounts for the difference in result of the same operation in similar cases. These comments necessarily apply to any operation which favors an advancement of the vitreous, lens and iris.

Reasoning, directly and by exclusion, from frequently ascertained and unquestioned facts, constrains to the conclusion that a condition always found in acute glaucoma, which will account for all its features without distortion, offers the true explanation of this form of disease, viz:

A great engorgement of the intra-ocular blood-vessels, overfilling the space within the sclerotic, most so posteriorly, about the entrance of the arteria centralis, the twelve to twenty short ciliary arteries, and the two long ciliary arteries which pierce the sclerotic at a right angle; elongating the corpus vitrei in the direction of the length of the vessels by lateral pressure which is magnified by the acute venous stasis developed by any slight increase of intra-ocular pressure upon the vena vorticosae as they pass very obliquely out through the sclerotic; and advancing the corpus vitrei, lens, and iris by pressure from behind, reducing the depth of the anterior chamber, and applying the iris to the cornea, thus obstructing the anterior channels of filtration,* after *increased intra-ocular tension* has been *produced.*

The *direct* course of the arteries through the sclerotic permits ready access of arterial blood, any increase of which, beyond what is normal with the eye, *must* exert some pressure upon, and stretching of, the sclerotic, which, in turn, narrows the lumen of the veins passing *obliquely* through it, still further increasing the intra-ocular



A vertical section of the eyeball from before backwards, enlarged five times. The white lines show the length of the channels of the vena vorticosæ (1½, 3¼, and 5½ mm.) relative to the thickness of the sclerotica, which is not usually appreciated. The channels do not extend directly back, but backward and downward. The proper anatomical entrance and exit of the longest channel cannot be shown in the profile.

pressure until stasis is absolute. Here we have "a vicious circle," but in a region different from that in which it has heretofore been located, and one capable of relief by the control of the primary

* "Making channels from 1½ to 5½ mm. in length." (Metz, Anatomy and Histology of the Eye, 1868, p. 35.)

extra-ocular influence, and without operation; which we so often see to be the case in the earlier attacks, called prodromata.

The engorgement of the vessels of the fundus oculi, existing in acute glaucoma always in direct ratio to the violence of the attack, conclusively shows it to be distinctly vascular in origin, which is extra-ocular. By reason of the high general arterial tension, and the quickened, forceful, action of the heart, the blood entering the eye, posteriorly most directly and in most volume, makes room for itself within the sclerotic by driving forward the solid moveable contents of the globe. A state of the system which leads to a reduction in the calibre of the peripheral arterial vessels, demanding an increased effort on the part of the heart, will account for this; because, as the contraction of the peripheral vessels diminishes the size of the blood-current passing through them, the propulsive efforts of the heart must increase, and these determine the volume of blood in the direction of *least* resistance. Therefore, the vessels which receive it are the intra-cranial vessels which have no vaso-motor constrictors, and those of the internal organs whose temperature is higher than the body-surface. Obviously, the cause must be some element in the blood which narrows the calibre of the vessels by irritation, aided at times by the contracting influence of low surface temperature, or by some emotion exciting a reflex from the base of the brain, or creating tumult of the heart.

Whether the intra-ocular vascular engorgement is ever excited by the precipitation of sodium bi-urate within the eye, or not, will probably be settled only by accidental observation. I think, not necessarily. It is more than probable that great emotion disturbing the regularity and stability of the heart's action, or a fit of indigestion with distension of the stomach and consequent reduction of the peri-cardiac space, when the heart is already laboring to overcome the resistance offered by the narrowed peripheral vessels to the passage of a normal blood-current, is the first step in acute action. In which event, the first indication is to relieve the heart of excessive work by dilating the peripheral vessels, which at the same time will divert the pressure of the blood-column from the intra-cranial vessels, from the intra-ocular vessels, and thus reduce the intra-ocular tension.

Chronic simple glaucoma differs so much from the other forms of the disease, and especially from acute inflammatory glaucoma, that some observers have doubted if it be glaucoma at all. It is glaucoma, a chronic interstitial ophthalmitis; a most perfect presentment of a chronic process which can be imagined, and is brought

about by the same initial influences which cause the acute form, acting without explosive force. As acute glaucoma is vascular and violent, this form is interstitial and slowly progressive. For years, its development is preceded by a stationary, or an imperceptibly increasing, general arterial tension, united with palpitating and uncertain action of the heart, and increasing rigidity of the sclerotic coat leading to the deduction that senility is an etiological factor. Age is a predisposing influence, as it is physiologically a period of substitutive fibrosis; if it were an active agent, we would find an increasing percentage of simple glaucoma with advancing age. A new connective tissue growth has, by anatomical dissections and microscopical examinations, been found in all the structures of the glaucomatous globe, and as a formative predominance of special tissues arises in specialized irritability of such tissue, for its cause we must look to some irritant exciting vascular and neurotic disturbances affecting nutrition. The presence of such an irritant, inherited or acquired, constitutes a *diathesis*. The preponderance of evidence, (ocular tissue-changes and symptoms, and the associated constitutional manifestations,) indicate glaucoma to belong to acquired tertiary syphilis (rarely), or to the diathesis termed *arthritic*, which includes gout and rheumatism.

These are congeners in their origin (inadequate digestion) and in their pathological expression—the modification and proliferation of fibrous tissue, and the irritation of serous membranes.

GOUT AND RHEUMATISM.

The two important factors in the arthritic diathesis, generated in the system and constant, are organic acids: uric acid, a product of inefficient proteid metabolism; in excess ("largely a renal question," Ewart), the cause of gout: and lactic acid, a fermentation product of the hydrocarbons (sugar); in excess (due to the condition of the integument), the cause of rheumatism. No uric acid has ever been found in the blood in rheumatism, and its excretion by the urine in the disease does not exceed the quantity usual in fevers. Haig believes both affections to be due to uric acid, to which Garrod and others demur. In acute attacks of both diseases there is chill, fever, and sweat, pain in the joints, a coated tongue, loss of appetite, thirst, constipated bowels, and scanty, high-colored urine which makes a red deposit on cooling, (most of which is a familiar picture in acute inflammatory glaucoma.) In rheumatism the fever is more marked, the sweat more profuse and acid (contain-

ing lactic acid), metastasis more common, and the joints seized in the first attack are larger, for even the peri- and endo-cardium, the pleura, the peritoneum, the spinal or cerebral meninges may be involved; for lactic acid is excreted by the urine under no conditions, beyond an approximately fixed quantity; it is not precipitated, no deposit ever having been found; nor is it known to combine tenaciously with any constituent of the blood. When in excess, therefore, *unless excreted by the skin*, it is retained in the circulation, and acts as an excitant; an *excitant*, for Gaskel found that when dilute lactic acid was injected into the circulation of a frog the calibre of the arterial vessels was enlarged, and the ventricle of the heart was relaxed. The action of dilute alkaline solutions upon the heart and the arterial coats was the reverse,—contraction. Lactic acid, denied passage through the skin by the constringing effect of cold and damp upon the dermal vessels, passes with the blood in greater volume to the deeper-seated organs of higher temperature, and excites violent action there. The larger the joint and the higher its temperature, the larger the volume of blood, consequently the greater the quantity of lactic acid which *will pass through it*, and the greater the stimulation. The lower temperature of the small joints, and the smaller volume and slower current of blood circulating through them, limits their exposure to the effect of lactic acid. The great excess of lactic acid in the blood in this disease, its saturation of the saliva, the sour (lactic acid) sweats, the purely conjectural attitude of the bacterial and the neurotic theories, and the suggestive habits and environment of rheumatics, continues to the lactic acid theory the prominence and probability which have belonged to it for some years. These are not diminished even by the failure of its treatment by alkalies, for, according to Sir W. Roberts, it is difficult to influence the reaction of the blood, requiring large quantities of acids or alkalies, and then the result is uncertain and temporary, owing to their prompt elimination by the urine. Moreover, "lactic acid is *formed* whenever sugar in solution is brought in contact with an alkaline, or earthy, carbonate in the presence of a special ferment, as casein." (U. S. Dispensatory, 1894, p. 66.) An excessive formation of lactic acid probably arises from the inefficient preparation in the mouth of the hydro-carbons, due to insufficient salivation, a subnormal percentage of ptyalin in the saliva, or the unfavorable conditions to which they are subjected (hot and cold drinks with food), for ptyalin acts only between 95° and 102° F. A low ratio of ptyalin, which the analysis of the saliva of some rheumatics has shown, taken with an

inherited delicacy of the skin, may account for an inherited tendency to rheumatism. The claim in favor of dampness and cold as initial causes, because rheumatism is more common in New England than elsewhere in the United States, and in Scotland and Ireland than elsewhere in Great Britain, happens to be coincident with the fact that in those sections the hydro-carbons, eaten in a manner least favorable to ptyalization, are a staple food.

The writer has dwelt at such length upon this subject, because rheumatism has so often been included with the uric acid diseases, which to his mind is clearly an error; because it is a part of the subject asigned to him; and because, in consequence of the excess of fibrine (sometimes twice the normal) in the blood in rheumatism, the affections of the eye due to it are apt to be *adhesive* in character: plastic, or parenchymatous, iritis may be due to rheumatism; serous iritis is of gouty origin.

Gout in its *articular* manifestations is a local affection of constitutional origin; abarticular gout, latent or declared, precedes the seizure of a joint, and the term gout should include all the baneful activities of uric acid in whatever part of the body they are met. Although, in addition to the very chronic process of fibrosis, which is the tissue-form ultimation of mal-nutrition, and due in part to an excess of urates in the circulation, a common feature of gout is the local deposit of sodium bi-urate, which may be frequently seen in the palpebral and bulbar conjunctiva, in the skin as tophi, as well as in the joints, and as Meyer (Fergus's translation, Diseases of the Eye, p. 248) states "in acute glaucoma the aqueous is muddy and sometimes forms deposits on the posterior surface of the cornea," which condition I have not observed. It is not easy to determine the character of such deposits, but I have held deposits in this situation following serous iritis under suspicion of being sodium bi-urate, though Garrod claims that the inflammation excited by their presence destroys such deposits; we do not find this true in keratitis punctata. As a deposit within the eye in sufficient quantity to be seen is not essential to its power to create excitement in so delicate a structure; as only irritation sufficient to fix the focus of vascularity when the heart is in exalted action from disturbed emotion, etc., is required to decide an acute glaucoma; a determination of the presence of such a precipitate would be inconclusive. Such investigation is beset by invincible difficulties. The urates, while remaining in the circulation, produce irritation of the fibrous tissues and serous membranes with which they come in contact,

and may thus decide a region for the concentration of any general vascular tumult, but they do not directly cause *acute* local trouble unless massed by precipitation, which is favored by the lower temperature of the small joints, their consequent comparative sluggish circulation, their composition of fibrous and serous tissue for which the *materies morbi* of gout has a predilection, and the injuries to which they are exposed. All of these conditions the globe of the eye satisfies.

The presence of a precipitate in the bulb not being a *sine qua non* to an acute glaucoma, an excess of urates in the blood, and palpitating action of the heart being sufficient to declare such an effect, we may accept as evidence of gout the existence of migraine, eczema, uncertainty of temper with insomnia, mental depression or hebetude, crackling of the cervical spine, pain in the gastrocnemiæ after a short walk; certain forms of scleritis, keratitis, and conjunctivitis, serous iritis, pulsating arteries and veins, increase of albumen in the aqueous, extravasations of venous blood, turgid and swollen ciliary processes, and great œdema; pharyngitis, cystitis, so-called idiopathic urethritis, herpes, or progressive deafness. The longitudinal ridges and broad lateral furrows, and the extreme brittleness of the finger nails are additional indications of the degenerating influence of the diathesis. The thread-test of the blood for uric acid, however, is crucial. Gout expressing itself in glaucoma has not necessarily other serious manifestations. I have never seen a glaucomatous person with a bald head.

The malaise and slight chilliness, followed by flushing of the face and mental stupor, so often observed in uric-acid-aemia, is not rarely mistaken for some form of malarial fever, as it may have periods of remission and recurrence within the twenty-four hours, to which error the beneficial effect of quinine in excluding the urates from the circulation, is contributory. An examination of the blood for the malarial parasite or uric acid, may be essential to a diagnosis. That no deposits of sodium bi-urate have been externally manifest does not justify the exclusion of gout as a cause of glaucoma, for gouty changes sufficient to destroy life itself have occurred without apparent joint deposits, or active inflammatory processes.

The known incidents of acute podagra and acute glaucoma, and their perfect mimicry, allowing for the function of the organs attacked, show each to be an "uric acid storm," the region being selected by reason of its individual specialized irritability, a tendency ordinarily inherited.

Sir William Roberts (Croonian Lectures, 1892, Uric Acid, Gravel, and Gout, pp. 33 and 119) offers a very fascinating suggestion in explanation of habitual excess of uric acid in a system.

'Structurally, no essential difference exists between the kidneys of birds and snakes, and those of the highest order of mammals, man: functionally, there has been immense evolution from the solid or semi-solid form to the watery form of urine, and in the substitution of a soluble form of nitrogen (urea) for one very sparingly soluble (uric acid.) This particular of physiological evolution has not yet been perfected, and man must still excrete 8 or 10 grains of uric acid a day.'

"In the course of such an evolution a double change would be in progress; namely a gradual substitution of urea for uric acid as the final term of proteid metabolism; and the complementary modification in the functional aptitudes of the renal cells,—that is to say, an ever-increasing aptitude for the excretion of urea, and an ever-diminishing aptitude for the excretion of uric acid. When, after long eons, the mammalian type was at length evolved, there remained only a small residuum of uric acid to be dealt with; and, correspondingly, only a small residuum of the original aptitude of the renal cells for its excretion. A feature thus begotten would present great variation in different individuals. Generators of gout, and members of gouty families, are, for the most part, people of fine frames and ample appetites, who are withal great consumers of nitrogenized food. In such persons there is an enhanced production of urea which expands by grams, while uric acid expands only by grains. There would thus arise a persistent demand on the urea-excreting faculty which could only be satisfied by an encroachment on the residuary faculty for the excretion of uric acid."

When he produces urea and no uric acid from nitrogenous food; and when from this he has assurance that "he eats to live" and not to die, man will probably have reached his physical millennium.

THE GOUTY AND RHEUMATIC DIATHESES WITH RELATION TO DISEASES OF THE EYE.

The Gouty and Rheumatic Affections of the Uveal Tract.

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I.

Affections of the eye are mentioned among the earliest of recorded facts in the history of gout.

Long before the gouty or rheumatic origin for other ocular lesions was inferred or established, *affections of the iris* were considered among the recognized complications of gout and rheumatism, such manifestations being formerly described under the general term of *"ophthalmia arthritica."* More recently, however, the careful study of clinical histories in typical cases has demonstrated conclusively that, not only in iritic disturbances, but also in certain other lesions of the uveal tract, gout and rheumatism must be considered as among the principal etiological factors (relapsing cyclitis, irido-choroiditis, exudative choroiditis, etc.)

These ocular lesions are in most instances associate manifestations of the maladies in question and start as such in one or the other part of the uveal tract, although less commonly they appear as complications of pathological expressions in other parts of the eye due to the same causes: (epi-scleritis, scleritis migrans, sclerotitis, neuritis optica, neuro retinitis, etc.)

Clinically, both gout and rheumatism are thoroughly understood. But however manifold and unmistakable the expression of local and general gout as well as rheumatism may be, it must be admitted that the obscure nature of both of these maladies, as well as the complete absence of a distinct morbid anatomy, are equally incontrovertible facts.

If this holds good of gout and rheumatism as a whole, it applies with especial force to the local manifestations of general disturbance that we meet with in ocular lesions. At the very outset, every observer of clinical phenomena in complications of the uveal tract presumably of gouty or rheumatic origin, is confronted with the ever vexed questions: "Are gout and rheumatism *independent affections* or are they, as Haig and others assume, different utterances of *one*

and the same malady, or is there such a blending of the two that their *common identity* must be upheld? Are we to believe with Hutchinson that "gout is but rarely of pure breed and often a complication of rheumatism"? How shall we classify that chronic affection of the joints, which, in its clinical manifestations at least, strikingly resembles rheumatism and gout,—arthritis deformans? These and other equally perplexing questions suggest themselves to the specialist from time to time. On the other hand, there are certain facts which his own observation, the literature of gout and rheumatism and the known experience of his fellow-physicians, have made him familiar with. These will serve to guide him in his endeavors to analyze the ocular symptoms and establish their dependence and association with the general ones.

In the first place, the examiner cannot fail to remark that while acute, sub-acute and chronic rheumatic seizures are of common occurrence, acute ocular manifestations, (for instance, acute iritis, choroiditis, etc.,) as associate expressions during and at the time of such acute or chronic exacerbations of the affections of the joints, are rarely or never observed. In other words, we can take for granted that complications of the uveal tract occur only in exceptional instances as simultaneous expressions with other typical manifestations of these maladies. On the other hand, careful clinical experience has shown that it is during the intervals of acute or chronic paroxysms of rheumatism and during the so-called goutiness period or antecedent gouty stage which precedes, for a variable period, declared or local gout, or during the interval between such attacks that ocular complications, and in particular, iritis and iridochoroiditis are prone to occur.

Guided by these and other established clinical facts, attention is directed to some of the pertinent queries which are suggested to us as specialists. Our personal deductions, based upon practical observations and experience, may not add much that is new, but they may tend to confirm or supplement many points in the history of gouty and rheumatic disturbances of the eye concerning which imperfect conclusions may have been entertained.

Can gout or rheumatism be considered principal etiological factors in those cases of iritis in which a searching examination fails to disclose that the disturbances of the joints are dependent upon syphilis, gonorrhœa, chronic lead-intoxication, malaria, anæmia and other actual or alleged constitutional causes?

This has long been admitted.

The older literature refers to these lesions of the uveal tract as

ophthalmia arthritica, iritis varicosa, arthritica, rheumatica, etc. Von Ammon, von Walther, von Beer, Himly and others are among the early German observers who refer to the frequency and severity of this special variety of iritis and assign its cause to gout or arthritis rheumatica. In England, although rheumatic iritis and its causal relationship with rheumatism is recognized, Mackenzie and others refer hesitatingly to iritis of gouty or arthritic origin, even though it is mentioned, admitted and described in their text-books. Within recent times in Germany, and on the continent generally, less stress is laid upon these causes as etiological factors, and this is evidenced by a scarcity of the literature on this subject and by the infrequent reference and even the complete absence of the designation "gouty, arthritic or rheumatic" iritis in most of the text-books and treatises. On the contrary, in England,* where formerly much doubt was expressed, especially concerning the gouty or rheumatic origin of certain forms of iritis and choroiditis, opinion has gradually changed.

To Jonathan Hutchinson, mainly, belongs the distinguished merit of having been among the first who, by painstaking labor and observation, accumulated such a mass of clinical evidence that the gouty and rheumatic origin for these and other affections of the eye, can no longer be questioned. Since then we know that many cases that were formerly described by the vague term "idiopathic" (respectively causeless) or were classified indiscriminately as of rheumatic origin, are really expressions of the uric acid diathesis and belong to the stage of goutiness (a variable period which precedes the local paroxysms); or again are evidences of the rheumatoid stage, with its common or uncommon manifestations, including many neurasthenic and neuropathic symptoms, oxaluria, intestinal indigestion, eruptive and herpetic lesions of the faucial and other mucous and cutaneous surfaces, and finally terminating in an acute invasion of the larger joints.

If, as is claimed, syphilis is responsible for 60 to 75% of iritic, ciliary and choroidal disease,—toxic or septic causes (gonorrhœa, etc.) for 5 to 10%, assuming that gout and rheumatism constitute at least 20% of the remaining portion (15 to 30%),—what share of this is assignable to gout as such, what proportion to rheumatism as such,

*Mackenzie mentions the fact that in Germany chronic arthritis and gout affections were common among the poorer classes, especially in wine-growing districts. Before the advent of reliable mydriatics, these affections, characterized by their insidious onsets, were fraught with great risk; an acute attack was almost invariably followed by recurrent attacks, fatal complications, with loss of sight, etc.

and lastly what portion to the manifestation which is a blending of both and is designated as rheumatic gout?*

Mr. Hutchinson assigns an important share to gout as an etiological factor, but a major share to what has been termed by him and others "rheumatic gout." The more purely a case is one of rheumatism, the less is the possibility that iritis will happen. When iritis occurs, the complications are almost invariably those which suggest what we call rheumatic gout than rheumatism pure and simple.

In this country, with its diverse and changeable climate, mixed population living amidst every condition of favorable and unfavorable hygienic surroundings, rheumatic affections are common. Basing this statement upon my personal experience, I affirm unhesitatingly that in America we meet with iritis and other choroidal complications which, on account of their unmistakable resemblance to that group, must be classed with "rheumatic" affections.

Under all circumstances, it is evident that in a certain number of cases the ocular disturbances mentioned represent a part of the group of symptoms which are an advanced expression of one and the same diathesis; on the one hand, in gout (acquired or transmitted in an attenuated form through heredity), the presence of uric acid in the blood and deposits of bi-urate of soda around the smaller joints, constituting the chief pathological alterations; while on the other hand, rheumatism, in its sub-acute or chronic form, is characterized by sudden inflammatory invasions of the larger joints. Among other deleterious agents, the same morbid product (uric acid) is present, but undergoes different transformation after accumulation in excessive quantities. As a necessary sequence, in both cases there are enacted peculiar changes which interfere with and prevent the metabolic processes, especially of the connective tissues and lymphatic channels. It follows from this that we may expect iritic and other complications of both maladies and also of that form which is a fusion of both, known as rheumatic gout.

2.

At what period are iritic and other lesions of the uveal tract apt to occur? Are they more common during the acute outbreaks of local gout and rheumatism, or during the latent periods of these affections?

*Unquestionably cases of iritis have been added to this category, which occur in the course of that chronic affection of the joints known as arthritis deformans, or crippling rheumatism. This disease, because of its symmetric deformities, etc., is looked upon as autroph-neurosis (allied to the arthropathies met with in chronic affections of the spinal cord) and should not be considered in this connection.

This subject has been referred to in another place. As a general rule, ocular complications appear during the early manifestations of the uric acid diathesis, or during the stage which precedes, for a longer or shorter period, acute outbreaks of either gout or rheumatism, or during the intervals of acute or subacute recurrent attacks.

In one of my cases, Mrs. F., 32, Piqua, O., a violent rheumatic seizure (affecting the larger joints,—ankles, knees and elbows) persisted for more than a year and finally disappeared without topaceous deposits or stiffening. Recently, five years after the first and only attack, she developed acute iritis of the right eye on a visit to the country after walking over damp grass. Amidst violent suffering and typical objective symptoms, this attack subsided rapidly. It was preceded for several months by neurasthenic disturbances, malaise, migraine, etc. In another case, under the clinical picture of so-called serous irido-choroiditis and unmistakable evidences of a uric acid diathesis, a most persistent disturbance, with frequent and violent relapses, came about. Seven years afterwards inflammatory invasion of the joints came about and persisted for more than a year. During this period the ocular symptoms were quiescent, but after the subsidence of the joint-affection, they recurred with violence. The patient came to me about this time. An iridectomy was at once advised and performed with temporary arrest of inflammatory activity. Since then repeated recurrences have taken place, and these have resulted in a low grade of chronic irido-choroiditis with dense precipitates on the posterior surface of the cornea but no tendency on the part of the coloboma to become occluded. The ultimate fate of this eye, as that of so many like it, will be its removal to avert uncontrollable inflammatory disturbance and suffering.

The question whether in exceptional cases iritis and choroiditis may be a simultaneous expression and prominent among the other clinical phenomena during an acute outbreak of either gout or rheumatism, has generally been answered negatively, and no reliable clinical data are to be found among the mass of recorded cases in the general literature of gout or rheumatism. It is never a simultaneous, though in exceptional instances it may be a concomitant, expression. If such processes are lighted up during the acute attacks, this must rather be considered a coincidence than otherwise.

The following observation is interesting because it bears upon this point. A woman, aged fifty, complained of a persistent burning sensation about the eye-lids. Her eyes had the typical hot-eye appearance so often seen among gouty subjects. A simple colly-

rium was advised. The following day I was sent for and found that a violent rheumatic seizure affecting the shoulders and hips had come about, with severe pain in both eyes. Examination showed marked epi-scleral injection, discolored aqueous humor and dusky iris. The interesting feature was, that under salicylates, hot fomentations and the usual local treatment, rapid subsidence with restoration of function followed.

3.

Do the ocular disturbances, and in particular the lesion which forms the subject-matter of this paper, offer any confirmatory evidences for any one of the many theories advanced to explain the morbid changes which affect the joints, tendons and fibrous tissues in gout and rheumatism?

We must admit at once that there is nothing distinctive in the pathological appearance of an iritis or irido-choroiditis by which it can be invariably recognized and connected with these constitutional maladies. A part or the entire category of symptoms, from the numerous manifestations (latent or otherwise) of the uric acid diathesis to the unmistakable gouty or rheumatic cachexiæ must be present before the ocular lesion can, with reasonable certainty, be assigned to these causes. Nevertheless there are certain local features which strongly suggest this origin even though there may be a lack of evidence on the part of the general symptoms.

So far as offering positive deductions concerning the morbid anatomy of gout, the pathological changes in this important tunic of the eye appear principally to attack the lymphatic circulation and the delicate connective tissue fabric, in this way resembling the great connective tissue disease, syphilis.

Can we differentiate between gout and rheumatic affections at any time during the progress of these maladies, and can we assign the greater share as an etiological factor for the iritic and other complications to one or the other?

During the prodromatic stages, or after the blending (local or general) of the symptoms takes place, it is impossible to do so. But during the early stages, before the characteristic alterations have affected the joints, either as the typical gouty joint or the typical rheumatic one, we as specialists can establish a more rational etiology in assuming one or the other or both as the origin for these lesions of the eye.

(1) During the stage (sometimes interminable, sometimes hardly

manifesting itself) before local gouty or rheumatic invasions of the joints occur, we can hardly speak of gout as such or rheumatism as such, but we must look upon these manifestations as goutiness, so-called, or as a rheumatic or rheumatoid tendency.

(2) After the malady declares itself, it may happen that its pure characteristics may be preserved for a long time, or even become permanent, so that the patient, on the one hand, presents only the typical gouty manifestations, or on the other hand, only the typical rheumatic evidences, so far as the joints and other general symptoms are concerned.

(3) In other cases again, as both progress or develop, one partakes more or less of the characteristics of the other until such an intimate fusion takes place that by common consent the term rheumatic gout has been selected.

In the following pages I have condensed the results of my personal experience, together with such deductions as clinical study has confirmed by repeated observation.

A. THE GOUTY AFFECTIONS OF THE UVEAL TRACT.

During the stage of goutiness, or latent gout before its declaration as an acute, painful disturbance of the smaller joints, especially of the foot and hand, we meet with annoying complaints, which are chiefly referred to the constant presence of muscæ volitantes. In most cases careful examination discloses a normal fundus oculi with unimpaired sight and function. In such cases we may find a passive congestion of the vessels, of the sclera and epi-scleral region, the typical "hot eye" appearance of the English, and again it may only be part of other neurasthenic disturbances, or of an overwrought state of the nervous system. Not infrequently these "muscæ" have a pathological importance and occur as prodromatic manifestations of exudative choroiditis.

A definite pathological expression of iritis is rare. It is more frequently met with as a complication of scleritis, epi-scleritis, disseminated sclero-choroiditis, and in exceptional cases it may be secondary to a lesion which primarily affects the retina, and secondarily invades the choroid, and vitreous humor. As a primary or an isolated inflammatory disturbance, "gouty" iritis is uncommon, and even in such cases, it is often found to be dependent upon a marked pathological process, which begins in other parts of the

choroid or ciliary body, and of which iritis is only the most conspicuous feature.

A far more frequent lesion is an insidious variety of exudative choroiditis, which appears under the clinical picture of so-called serous iritis, or irido-choroiditis, usually occurring during the initial stage of gout or during the intervals of acute attacks.

Of all the obscure ocular lesions caused by the outbreak of gout, this is the most treacherous. Muscæ volitantes, functional disturbances of vision, subjective "glimmering," luminous appearances, etc., are present for months when the so-called iritis serosa is added. The clinical picture now reveals precipitations on the posterior surface of the cornea, sero-plastic exudation in the anterior chamber and on the surface of the iris, posterior synechiæ, floating opacities in the vitreous humor, especially in the anterior portion, and deposits on posterior lens capsule. Progressive failure of vision and most annoying subjective disturbances are usually present. In rare cases the tension may become reduced, in others and far more frequent it is increased, terminating finally in secondary glaucoma.

The local treatment requires the greatest discrimination. Mydriatics are dangerous: myotics also: cocaine is useless. Benefit may result from the application of moist heat or hot irrigation against the moist lids. Paracentesis of the anterior chamber, repeated daily according to indications, is in many cases a beneficial measure. If, in spite of this, the tension remains increased an iridectomy or a sclerotomy may become necessary.

The indiscriminate use of the remedies ordinarily indicated and resorted to, may result in positive harm. An active, internal medication of colchicine, salicylates, etc., hot baths, together with the local application of moist heat supplemented by paracentesis corneæ, and the cautious use of either myotics or mydriatics according to indications in weak solutions, may alone avert enucleation, which in many cases becomes finally the only measure of expediency to rid the patient of an interminable and incurable affection.

In the more favorable cases recovery ensues with impairment of vision; in others one or more scotomata are left, especially if the goutiness develops into declared gout. This is almost the rule, and if a persistent, chronic, degenerative process affecting the entire uveal tract is excited, the process terminates with atresia pupillæ, cataracta complicata, etc. V=0.

This lesion of the uveal tract is in my experience the most frequent expression of the gouty diathesis. It is as obscure as the

nature of gout itself. It manifests itself as a serous or sero-plastic inflammation-product of low grade, accompanied by chemical changes in the composition and quality of the vitreous and aqueous humors. The alterations in the anterior chamber and iris only mask the real lesion, which consists of single or multiple exudates into the choroid near the equator or in the anterior portion of the choroid and ciliary body.

Another, but less frequent, lesion is iritis associated with zona ophthalmica, or herpes zoster ophthalmicus.

This may occur in subjects, especially males, with inherited gout, or as an advanced expression of goutiness, or during the intervals of declared gout. We must differentiate between iritis which is primary and that which is secondary to the eruption of herpetic vesicles on the cornea associated with eruption along the course of the frontal divisions of the ophthalmic divisions of the trigeminus.

Another rare expression of the gouty diathesis appears under the guise of a low grade of iritis, or of the serous irido-choroiditis already referred to, but which is here secondary to degenerative changes which affect the retina and result in glaucoma. Iridectomy in such cases, although indicated, is fraught with danger. Equally rare are those cases, unquestionably also of gouty origin and manifesting themselves during the later periods of confirmed chronic inflammatory glaucoma, (frequently unilateral,) in which the most experienced surgeons as a measure of rational empiricism would first propose an iridectomy rather than immediate enucleation. Fatal hemorrhage from the retinal and choroidal arteries, followed by almost instantaneous extrusion of the contents of the globe, is rather a depressing experience, but one which many have encountered (and which has been reported in some instances and perhaps left unrecorded in even a larger number.)

We have also to refer to the gouty diathesis as one of the causes for glaucoma. The subject is of such interest and requires such extensive consideration that it is impossible here to make more than a passing reference to the fact that, among alleged causes for glaucoma, the source and origin is placed in the iris-angle and lymphatic spaces of this locality.

In this connection the brief history of two cases is given, both women with double non-inflammatory glaucoma. In the first case the iridectomy that was made was large, key-hole shaped, with clean sharp-cut limbs of the coloboma in both eyes. For months before the operation the disease was kept under control by the use of eserine, and because of the controlling effect of the myotic and the

favorable appearance of the external and internal structures, an operation for permanent relief was undertaken. Operative interference resulted disastrously: a chronic iritis or irido-choroiditis, due doubtless to miliary hemorrhages in the retina and choroid, hopelessly undermined the sight in both eyes.

The second case is at present under observation. Double iridectomy, clean and smooth, was followed in eight weeks by low grade of iritis and irido-choroiditis in both eyes, resulting in complete abolition of sight in the right eye and with a fragment of vision remaining in the left eye.

I believe that in both cases a gouty origin was responsible for the glaucoma and directly so for the disastrous complication, although no general manifestations of gout were present, either before or after the operation.

I believe that these cases are identical with those experiences (fortunately rare) which some oculists have had after an operation for the extraction of mature cataract, which from all external indications, perfect functional tests, etc., promises favorable results. The operation as such is smooth and uncomplicated. During the operation or immediately afterwards, however, successive hemorrhages occur in the retina and choroid and vitreous without exciting any active disturbance. The healing of the wound is uncomplicated and no visibly unfavorable reaction comes about. But when finally the sight is tested vision is found =o. Several years ago an experience like this happened to me in a woman with "rheumatic gout." Uncomplicated extraction of cataract was followed by uneventful healing. Eight days afterwards, after insisting that she must be able to count fingers which she as persistently stated she could not do, I was finally convinced of her inability when ophthalmoscopic examination disclosed the vitreous full of hemorrhages and retina and choroid detached.

In concluding this part of the subject, I give the history of a case which, as far as my experience is concerned, is exceptional.

Mrs. McM., æt. 47, Moscow, Ohio, was attacked during the night with excruciating pain in the left eye, which lasted for several hours attended by profuse weeping, photophobia, but especially great suffering when she attempted to move the eye.

On the following day the patient came to me for consultation. I learned that she had just passed the menopause amidst great nervous strain and suffering. She was a confirmed neurasthene, had had herpes zoster, eczema, migraine, in fact she showed every evi-

dence of the so-called uric acid diathesis, but no patent gout or rheumatic disturbance. The history of any former eye trouble was absent and from her account my first impression was that she had acute glaucoma. The examination, however, revealed a different state of affairs. The lids were glossy, tense and swollen. The ocular conjunctiva was intensely congested and chemotic; the sclera bluish-gray; aqueous, discolored; pupil contracted and sluggish; iris dull; globe exophthalmic, with an appearance resembling incipient panophthalmitis; motion in every direction visibly constricted and excessively painful; complaints of nausea on attempting to open eye to look at objects; tension not influenced; moderate dilation of pupil after a drop of atropine solution. Ophthalmoscopic examination disclosed precipitates on anterior capsule of lens and posterior surface of cornea and exceptionally pronounced optic neuritis with enormous swelling and œdematous infiltration of the adjacent retina.

During the following days, amidst recurrences of suffering which in character resembled gout, on account of the exquisite sensitiveness of the lids and the attendant constitutional symptoms, the globe became almost immobile and moderate proptosis remained for several days.

Under anodynes, absolute rest, leeches, atropine, the iritis and swelling of the external parts subsided in eight or ten days, but any attempt to move the globe was attended by pain for weeks. The optic neuritis subsided slowly and complete restoration of sight came about.

The patient was seen recently and has had no recurrence.

It can be asked: "Was this an attack of acute iritis in a gouty or rheumatic subject with optic neuritis—a complication which we know is not uncommon? Was it angio-neurotic, or a sudden vaso-motor paralysis of the tissues of the orbit? Was it a sudden obstruction in the lymph channels, or in the cavernous sinus, or was it a local expression of gout?

Gout is infrequent among women, even though goutiness is not. It is admitted that these disturbances are more frequently met with after the menopause.

B. THE RHEUMATIC AFFECTIONS OF THE UVEAL TRACT.

We not infrequently meet with lesions of the uveal tract in which a distinct history is obtained which conclusively suggests either a rheumatic tendency without acute disturbances of the joints, or

positive inference that one or several paroxysms of declared rheumatic paroxysms had preceded the ocular disturbance. Such manifestations, in character resembling those met with during goutiness, may precede or follow the active local rheumatic invasions of the larger joints, and we are almost constrained to admit their rheumatic origin.

If such active paroxysms assume all the other characteristics which force us to assign them to the rheumatic group as such, before blending with gout rheumatic arthritis has taken place, we can furthermore determine that it is during the period of unknown duration which precedes the acute local attacks, or during the intervals of the recurrent ones, that lesions of the iris, ciliary body and choroid are apt to occur.

Just as in gout ocular disturbances rarely or never occur during acute or sub-acute rheumatic invasions of the joints.

The designation rheumatic has always been a vague one for reasons that are evident. There is no morbid anatomy, therefore all conclusions concerning its real nature are based upon speculative knowledge, supported, it is true, by a mass of clinical facts.

In the search of a rational etiology for the lesions of the iris and choroid, when all other known causes have been excluded, we must assume, in the absence of more positive proof, a so-called rheumatic tendency. Although we do not know what the rheumatic tendency is, we know with much more certainty what it is not.* We are reminded of the variation of an old German saying: "Was man nicht definiren kann dass sieht man als ein Rheuma an."

Goutiness as such has a more or less definite expression: the rheumatic tendency has no end of expression because it includes almost every known and unknown clinical manifestation.

The well known etiological dependence of rheumatic seizures on syphilis, gonorrhœa, septic and toxic disturbances, malaria, anæmia, demands of every specialist a most stringent examination of the real cause. In this rheumatism differs from gout; with the

* Ordinarily it can be said to be present with other evidences indicating metabolic changes in different parts of the body when we find a sensitive, nervous organization with greater susceptibility to taking cold, mental and emotional depression, tendency to acute attacks of follicular sore throat, lumbago and neuralgia in general, etc., etc., which, amidst certain exciting moments, exposure to sudden changes of temperature, excessive humidity, prolonged mental strain, excessive use of the eyes, or exposure to bright light, may be regarded as the foundation for acute inflammatory disturbances of the uveal tract.

latter struma, phthisis, herpes zoster, glycosuria are known to be correlated occasionally; the former, besides its own clinical peculiarities and intrinsic characteristics, is often only the conspicuous local expression of a number of constitutional diseases.

Among the early manifestations of the rheumatic diathesis in this part of the eye, the uveal tract frequently participates and functional derangements of the ciliary muscles, or distressing asthenopic disturbances, are observed.

The most frequent inflammatory affection of the uveal tract due to this cause is iritis, acute and chronic. In its acute plastic variety it may be insidious, and in some cases again it is only the most conspicuous expression of a general irido-choroiditis, and in others, less common, its onset is sudden, its course more rapid and symptoms more violent.

Another more accentuated expression of plastic iritis is occasionally met with. The onset is sudden, the course is stormy and suffering intense. Amidst local symptoms so violent that at first a parenchymatous or suppurative variety is suggested, an acute plastic process takes on exceptional characteristics. The anterior chamber becomes filled rapidly with an opalescent, grayish-yellow exudate of plastic lymph which completely fills the chamber. As the inflammatory symptoms disappear this yellow exudate subsides, and generally it can be observed to contract around a central point which appears agglutinated to the anterior capsule in the middle of the moderately dilated pupil. Another feature of interest is, that synechiæ are not as common as one would be held to infer from the apparent severity of the attack.

The chronic variety, either as an expression of general irido-choroiditis, or as the result of an acute process beginning and confining itself to the anterior portion of the uveal tract, is, with all its unfortunate consequences, one of the most dreadful lesions.

Cyclitis is not uncommon. It is particularly met with in young girls or in early womanhood. It is generally associated with sclerotitis or its milder equivalent, epi-scleritis migrans.

The pathological expression of exudative choroiditis, which starts in the choroid and under the picture of so-called serous irido-choroiditis or serous iritis, is quite common. It is not only destructive to vision, but the chronic, degenerative irido-choroiditis which is excited, with special tendency to hemorrhage and exudative extravasations into the choroid, retina and vitreous humor, frequently renders enucleation necessary.

C. AFFECTIONS OF THE UVEAL TRACT, ASSOCIATED WITH RHEUMATIC GOUT.

It can be held that in this group, which is a blending of gout and rheumatism, lesions of the uveal tract and iritis in particular, may occur.

It possesses no distinctive local characteristics, but because of the characteristic changes of the joints, the diagnosis of the ocular lesion is almost suggested by the appearance of the patient.

My own observations have familiarized me with several typical instances setting forth iritis as one of its complications. Cyclitis and choroiditis are not so common.

If iritic and other complications occur in persons with acute or chronic affections of the joints, in whom syphilis, gonorrhœa, chronic lead poison and other recognized causes are found, is it more apt to occur if such persons are gouty or rheumatic?

This is an interesting point to determine. Mr. Hutchinson has answered this question for us. It demands and awaits further corroboration. In the only case of gonorrhœal rheumatism which has come under my observation a gouty history was obtained.

My experience has been too limited to express a definite conclusion concerning other causes, but I incline to the opinion that a gouty or rheumatic heredity is of considerable importance in exciting or increasing the tendency to iritic and other complications.

THE GOUTY AND RHEUMATIC DIATHESES WITH RELATION TO DISEASES OF THE EYE.

Rheumatic and Gouty Affections of Conjunctiva, Cornea, and Sclera.

BY R. A. REEVE, M.D.

of Toronto, Canada.

Although Knies' judicial finding may be the true one, that it is rarely possible to prove the essentially rheumatic nature of an eye affection, it is equally certain that the materies of gout and rheumatism is an oft-present element in the human economy, and that the eye does not escape its baneful influence. It doubtless determines the onset of eye disease and also modifies its character and its behavior under treatment.

The prevalent disregard of wholesome hygiene, despite the widespread knowledge of its precepts, warns us that we cannot afford to ignore the part played in the etiology of ophthalmic diseases by arthritism,—"that diathetic habit of the body from which arise as branches two main and distinct classes of disorder, commonly recognized as gout and rheumatism." (Duckworth.)

A mere glance with the ophthalmoscope may settle diagnosis and prognosis, but the key to the common superficial ocular ailments may not always be so readily found. Jonathan Hutchinson affirms that many cases of irritable, hyperæsthetic and easily-tired eyes occur in association with inherited gout; and there seems need to pay heed to the warning of this great clinician, that we too often treat the eye as "a mere optic rather than as an organ." Risley found that many asthenopes were subjects of the uric acid diathesis.

THE CONJUNCTIVA.

While the conjunctiva takes part or is involved in inflammation of the cornea, sclera, and intraocular tissues, Fothergill holds there are no peculiarities that point to a conjunctivitis proper of arthritic origin. Even in such a seemingly local disease, however, as simple conjunctivitis it will be well, with Garrod, to get, if need be, what clue we can, as well as benefit, from systemic medication, for the choice of suitable local remedies may hinge upon a possible dys-

crasia. Experience shows that sometimes astringents, e. g., are resented or are ineffective where the indication for their use has seemed plain, and milder remedies, alkalies et al., replace them to advantage. Utilizing all means of diagnosis, we may at times get a hint by inspection of the mouth. The vascular, swollen and spongy gums bleeding readily and parting from the teeth,—a form of gingivitis and pericementitis now recognized as due to gout (or the "goutiness" of Ewart), with in some instances a marked tendency to deposits of so-called tartar, afford at times a ready and convenient sign. Not without meaning also is atrophy of the gums, the free margin of which has evidently receded from its original line, either as a result of simple inflammation or pyorrhœa alveolaris.

Arthritic Conjunctivitis (Gonorrhœal).—Haltenhoff dwells upon a benign form of conjunctivitis in connection with synovitis. He quotes A. Fournier, who first described minutely, as a variety of "ophthalmie rheumatismale," a conjunctivitis "accompanied by slight irritative symptoms and scanty catarrhal secretion" in the subjects of specific urethritis. He also cites Hirschberg, Prof. J. W. White, of Philadelphia, and others who with himself held to the "pathogenic connection between the conjunctivitis and the urethritis." Cheatham reviews the subject and gives cases of his own, with citations from various writers. The recently accepted theory regarding the toxic origin of this and kindred affections, which Cheatham supports, practically accords, as he shows, with the etiology advanced by Haltenhoff. The statement of Haltenhoff, that a few of these cases of conjunctivitis have been observed *without* rheumatoid symptoms, agrees doubtless with the experience of others. The writer reported its occurrence at a meeting of the Toronto Medical Society many years ago. He has seen four cases of benign conjunctivitis without rheumatism in the subjects of gonorrhœa, where the latter could be fairly considered causative. The attack resembled a mild catarrhal conjunctivitis with undue chemosis, and subsided in a few days. In the fourth case only, which occurred during the first attack of gonorrhœa, was the discharge yellow, but the gonococcus could not be found. Recovery ensued in a few days under mild treatment, with recurrence for a brief period three weeks later. There are various cases of inflammation of the palpebral conjunctiva and of the bulbar which, from their nature,—patchy and obstinate, may be fairly assigned to the arthritic diathesis. And the latter is doubtless a factor also in some cases of blepharitis.

DeWecker notes, what all have observed, the occurrence of conjunctival hemorrhage in the gouty, and emphasizes its prognostic import. "Chalky deposits giving the murexid reaction are sometimes found in the conjunctiva, and should be searched for."* Swanzy believes they occur more frequently than is ordinarily supposed, while in the experience of Sir Dyce Duckworth they are of extreme rarity. Jonathan Hutchinson says "little or no evidence exists as to the deposit of urate of soda in any of the structures of the eye."

CORNEA.

Keratitis rheumatica (Arlt).—Arlt describes a transient cloudiness of the cornea, with chemosis and irritability, which disappears in a few days and as a rule leaves no trace. Risley records an instructive case in point, with shedding of corneal epithelium, and rapid recovery when the hip-joint became affected. Fœrster also described an interstitial keratitis with acute articular rheumatism, doubtless toxinic. Its occurrence, though very infrequent, is in accordance with the statement of Prof. Pflüger, "all of the infectious troubles which may lead to uveitis may also lead to parenchymatous keratitis."

Ulcerative Keratitis.—Jonathan Hutchinson states: "In men, the subjects of acquired (and inherited) gout, we sometimes see acute and very painful ulceration of the margin of the cornea of a definite gouty nature, and curable by treatment suitable to that diagnosis. It may occur repeatedly in the same patients, and it usually subsides quickly under active treatment for gout. Women are not wholly exempt."

This condition would seem closely allied to, if not identical with, the so-called catarrho-rheumatic ophthalmia, of which we hear but little specifically nowadays, but the entity of which the great Scotch ophthalmologist, Mackenzie, insisted on many years ago in his classic work: corneal ulceration progressing from the periphery inwards "was extremely apt to occur," and was a serious complication, if not an essential feature, of the disease.

Horstman has observed in eyes, otherwise normal, band-like opacities of the cornea. This appearance alone, he says, always gave rise to a suspicion of gout.

Jonathan Hutchinson and Nettleship do not hold this view of their etiology.

* T. D. Pryce, Clin. Soc. Lon., Jan., 1893.

Sclerotising Keratitis.—Deep circumscribed inflammation of the cornea (deWecker).

When the cornea is involved by continuity in scleritis (sclero-keratitis) the infiltration at times "appears as centers which have a peculiar proneness to sclerosis." There results a porcelain-like irregular opacity of the cornea as if the sclera had encroached on the former. The affection is generally met with in persons over forty years of age, of rheumatic diathesis. It is also marked, as a rule, by extreme indolence and absence of any tendency to abscess or ulceration. There is pain only when the uveal tract is involved. The infiltration process can be arrested, but the sclerosed patches of long-standing are indelible. DeWecker lays stress on the value of pilocarpin hypodermatically (sweating course) and eserin as a collyrium and hot fomentations; also potass. iodide internally at the same time. To arrest the keratitis and reduce the sclerosis, deWecker advises sclerotomy. Less seldom there is a mild peripheral keratitis with the scleritis, which leaves nebulæ or else disappears. Other forms of keratitis may occur in arthritic subjects; for example, Burnham* reports a case in which "the center of the cornea was studded with closely-packed and small infiltrations: no iritis." In this instance marked benefit followed a thorough and repeated trial of pilocarpin injections. The writer has seen in a seemingly healthy young adult of distinctly arthritic ancestry, where eye-strain and other local and systemic causes could be excluded, a linear "salmon patch" on the limbus, lower temporal, making an arc of two lines with a fine gray infiltration of cornea 1 mm. wide: no general or ciliary congestion; media clear; vision perfect; eye free from irritation and the fellow unaffected. The same condition, only in miniature and transient, showed on the opposite side of the cornea. In about six weeks a similar smaller arc was found at the lower nasal margin of cornea, with no sign of the first one, and there was also a fac-simile near the summit. Reference would here be made to a class of cases at times associated with arthritis, so-called keratitis punctata, and the descemetitis of some authors, but that they are now included as a variety of uveitis.

EPISCLERA AND SCLERA.

Episcleritis proper, a circumscribed inflammation of the subconjunctival tissue occurring at one or other point in the anterior

* Can. Pract., Aug., 1892.

scleral zone, often about the insertion of a rectus, is held by some authorities to be a superficial scleritis, as Arlt, Nettleship, Hutchinson, Fuchs, deSchweinitz, but is distinguished by Noyes and Berry. By the latter, because "the inflammation is mainly or entirely confined to the loose episcleral tissues." At times there is but a slightly raised dusky red spot, akin to a conjunctival phlytenule; more often a firmly-seated dense elevation more or less nodular, or again mound-like, simulating a bulging of the sclera itself, and of a rusty look, within a highly vascular area of from four to five lines in diameter. The patch may reach the cornea, but the latter is hardly ever involved. The exudation always undergoes resorption, never ulceration, and, as a rule, after several weeks, subsides slowly, leaving finally a small slate-colored spot on the sclera which may pass away in a few weeks or abide. The affected eye may be irritable, but is rarely painful. The tendency is for several discrete nodular swellings to occur in succession, each one taking several weeks to develop and somewhat longer to disappear, so that at times three can be seen in different stages. Thus the disease covers several months, but leaves the eye practically uninjured. The most chronic case in my own experience was one where there were ten such, the vicinity of one rectus insertion after another being involved in rotation, with healthy intervening tissue, two and a half times around the cornea.

Episcleritis occurs most usually in adults. Some subjects are rheumatic, some gouty. Berry regards it as a decidedly rheumatic or gouty affection. DeWecker refers it to chronic rheumatism, and Meyer believes it to be almost always of rheumatic origin.

Episcleritis proper, with a "single dusky nodule at some little distance from the corneal rim," Jonathan Hutchinson attributes to inherited gout, and calls the nodules a form of "gouty chilblain."

In the milder cases of episcleritis, weak collyria of eserin or pilocarpine and massage with ungt hydrarg. ox. flav. (Pagenstecker) are in order, and subconjunctival injections of soda salicylate, sodium chloride, expedite recovery. In sub-acute attacks, soda salicylate internally and locally is of distinct value, and atropine and hot compresses may be required. A course of pilocarpine sweatings decidedly promotes resolution, and potass. iodide has proved very useful. Colchium gives relief in gouty subjects. Peritomy is beneficial in chronic recurrent cases, where the limbus is much involved (Berry, Sym, etc.). When there is much infiltration with pain, incisions even to the sclera have a good effect (Adamük, Gruening). Curetting is of advantage in selected cases (Schœler).

Any error of refraction or anomaly of extrinsic muscles should be corrected (deSchweinitz).

Panas regards so-called tenonitis as strictly rheumatic and akin to hydrarthrosis; its seat being not in the capsule itself but in the fine trabecular tissue which exists between the sclerotic and the capsule proper. Accepting this as a transient posterior episcleritis, and therefore fairly within our province, the writer recalls a pronounced case of undoubted character in an elderly female, the subject of well-marked rheumatic gout; pain, proptosis and chemosis, characteristic symptoms, were present. In these cases antilithic treatment gives speedy and decided relief, and recovery ensues as a rule within a week. It is interesting to note the protective immobility of the globe to secure rest, not explicable by the amount of effusion, which confirms the joint-like nature of the eye-ball with its investments.

Episcleritis periodica fugax (Fuchs).—This affection recently brought into notice by Fuchs was first described, as Fuchs himself states, by Jonathan Hutchinson under the name of "hot-eye."* The account the latter gives is as follows:

"Amongst the frequent occurrences which denote the presence of quiet gout, are repeated short attacks of congestion of the eye. Usually one only is affected, but sometimes both. The conjunctiva becomes red, and the eye feels hot and pricks as if sand were in it. The attack may come on within half an hour of the meal which has disagreed, and it may last a few hours or a day or two. Vision may be dim, and all attempts at accommodation are usually painful. In the intervals of the attacks the eye is usually quite well, and it is indeed its definitely paroxysmal character, its sudden development and very complete and rapid disappearance which especially mark its arthritic relationship."

Risley. "Lithæmic eye affections." "Intense hyperæmia of conjunctiva, eyeball tender." In twenty-four hours, under antilithic treatment, all discomfort removed.

Episcleritis periodica fugax, according to Fuchs, "consists chiefly in severe inflammatory œdema of the episcleral tissue, with active hyperæmia often attended by severe photophobia, lachrymation, pain, which frequently herald it." There may be only a violent congestion of the tissues.

The attack lasts from one to eight days, and may pass from one eye to the other and reappear in the same eye several times. The

* Bowman Lecture, 1884.

duration of the disease is, as a rule, some years. Fuchs reported only seven out of twenty-three cases cured. He considered treatment very ineffective. Men of middle age are most often the subjects. He found the uric acid diathesis present in a few cases, but could not trace gout. Wagenmann assigns gout as the cause, and Pflüger confirms this opinion. Critchett regards it as of rheumatic origin, and finds great benefit from quinine, salicine, hot fomentations and sweatings. Priestley Smith thinks it due to gout, rheumatism or faulty elimination of some sort.

Sydney Stephenson* gives a series of cases of episcleritis periodica fugax in young subjects, female almost without exception and free from the rheumatic or gouty diathesis. He regards change of air as more efficacious than any treatment by drugs, systemic or local.

Scleritis.—Scleritis now and then involves the whole ciliary zone (acute diffuse scleritis), less seldom a patch in the anterior part of the sclera (s. circumscripta), which may equal the cornea in size is of bluish-red color and somewhat raised, owing to subconjunctival infiltration, but not nodular as in episcleritis proper. Unlike the latter, too, which is usually free from pain, it is painful, at times markedly so, even without iritis. Moreover, iritis is more apt to occur and the cornea to be involved, sclero-keratitis, or the rarer, more decided, sclerosis, sclerotizing keratitis. It is given to relapses and chronicity, and different spots around the cornea may be attacked in succession. Finally at the end of weeks or months it terminates by resolution, leaving a dusky or slate-colored spot or zone marking the site of the diseased area. Sym calls attention to two favorite sites for scleritis, at the temporal side of the cornea and above its summit. There are transition forms between episcleritis and scleritis (Nettleship, Fuchs, Noyes). We exclude from consideration inveterate and malignant types, mostly in subjects of scrofula or hereditary syphilis, "scrofulous sclerotitis," found as a rule in adolescents or young adults, in which, owing to inflammation of the cornea, iris, choroid, vitreous, etc., with the sclera, with relapses from time to time, there results in the course of months or years a blind, misshapen organ (staphylomatous, pear-shaped, glaucomatous, etc.). And the second eye may follow suit. In those cases connected with the rheumatic or gouty diathesis and with gonorrhœal rheumatism, the "form and function" of the eye are as a rule unimpaired.

* Medical Press and Circular, London, 1896.

Even in severe cases, where there have been iritis and keratitis, the eye may remain practically useful. It is thought by many that the choroid is affected as well as the sclera, though no signs of uveitis may be patent; and it is held that the scleritis is an extension of the process. Fuchs, however, affirms that the pathogeny is not settled.

TREATMENT.

As in other developments of rheumatism and gout, careful attention to hygiene, including of course dietetics, is of special moment, partly in view of the obstinacy of the disease, and partly on account of the tendency to recurrence.

In rheumatoid or mixed cases, soda salicylate is very useful, not only as a corrective but also as an anodyne. Similarly, salol with or without phenacetin, etc., is of service. Potass. iodid. can be given at the same time with benefit, and is also of advantage as the disease is waning; arsenic is also useful in the later stage. During the acute stage of attack in gouty subjects colchicum would seem the remedy par excellence. Haig, however, says that it only acts in the same way as an alkali, and holds that its use has some drawbacks.

There can be no doubt of the value in many cases of pilocarpine, given in doses to cause profuse perspiration daily or on alternate days, and preferably by hypodermic injection. In his Ocular Therapeutics (1879) deWecker, who used this remedy with or without exhibition of mercury and potass. iodid., singly or combined, as indications pointed, says: "It exerts a powerful influence, and may be continued for weeks if only the hour at which the doses are administered be so arranged as not to disturb digestion. The injection, therefore, is best given in the morning on an empty stomach, while the patient is in bed." Others choose the evening hour, and aid the effect of the drug by hot drinks, etc. Sym* thinks its efficacy is undervalued by the profession. In cases of iritis atropine is, of course, in order, and hot fotus. Dry heat, as by the Japanese hot box,† is, in the writer's experience, sometimes preferable and more effective. Subconjunctival injection or soda salicylate, physiological salt solution, etc., is a line of treatment whose value is uncertain, but worthy of testing. It is less effective than in episcleritis proper.

* Am. Jour. Med. Sci., No. cxii.
† Advocated by J J. Chisholm.

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Discussion.

Dr. J. M. DaCosta, of Philadelphia.

Mr. President and Gentlemen of the Congress: I have but few remarks to make, and they will be rather from the point of view of a general physician than relate to particulars in reference to the special subject so fully before you already. Concerning the eye diseases that are noticed in gout, in rheumatism, and in rheumatic gout, I think it is well to first consider what these maladies really are.

As regards rheumatism, we all know the typical phenomena of acute rheumatism; there can be little doubt as to whether a person has an acute rheumatic disease, but there is great doubt always with chronic rheumatism. I fully believe that more than one-half of the cases we call chronic rheumatism are not rheumatism at all. We must closely scrutinize them in connection with eye diseases as well as with other disorders. I have not the least doubt that in process of time what is now designated chronic rheumatism will be subdivided until there is little of it.

When we come to gout, the case is clearer. We know much more about the pathology of gout than of the pathology of acute rheumatism; and, whether it be cause or effect, it is quite certain that something connected with over-formation or faulty elimination of uric acid is at its root.

As regards rheumatic gout, I, for one, do not believe that there

is, strictly speaking, such a disease. There is a disease that may be called rheumatoid arthritis, or arthritis deformans. So far, we know almost nothing of its pathology; it is an affection in which the joints enlarge, in which uric acid is not found in the urine in abnormal amount, and which is not connected with rheumatism or gout, though it is not uncommon in those of rheumatic tendencies.

Now, from the point of view of the physician—I have little knowledge of the details from an ophthalmological point of view—I ask myself this question: In acute rheumatism, under what circumstances have I met with affections of the eye, particularly inflammatory affections, conjunctivitis, iritis, etc., such as the general practitioner recognizes, and then turns over to the ophthalmologist? The one I have generally found is conjunctivitis, with, sometimes, iritis, and I have noticed that this occurs during the attack of acute rheumatism,—that is, that it forms a part of the attack, and often at its height.

In gout, the case is different. The inflammation of the eye happens not during the acute seizures of the disease, but ordinarily when no such attacks exist. And here again, taking only my general knowledge of the subject as a guide, I find that it is usual to have this inflammation of the eye,—I am speaking more particularly of conjunctivitis,—originate first in one eye and then go to the other; or one eye alone may remain affected. I have so often seen this in gouty people that I have learned to associate it with the disease. In gout we may also encounter hæmorrhagic retinitis, and iritis which is prone to relapse. We may, too, meet with chalky deposits arranged along the small blood vessels of the conjunctiva. In all cases it is important to examine the urine to see that there is no co-existing kidney lesion.

Turning to the third division, if you can call it a division, I will put the question from the standpoint of a general physician. Are these acute eye affections in so-called rheumatoid arthritis, common? and I answer no. During a long experience, I can scarcely remember an association of the kind with pure rheumatoid arthritis. There is in this a point of distinction between it and rheumatism and gout; and just as we know that acute diseases of the heart do not happen in rheumatoid arthritis, so I maintain that acute diseases of the eye do not happen. I call the attention of the gentlemen of the Society to this matter, and their larger opportunities will enable them to solve the problem.

One more point to which my attention has been much called is, that there are a certain number of people having what is called sup-

pressed gout, or, better, lithæmia—a form of gout if you like, but without acute general symptoms. Yet here the eye inflammation is sometimes very acute; and it has been a matter of great interest to me to make in these patients the same observation that I have made in the case of gout pure and simple, namely: that the eye inflammation begins generally in one eye, and then attacks the other. I have seen lithæmia with marked headache followed by the eye affection, and the reverse. I have also often known persons to be treated for eye disorders and then all turn out to be due to lithæmia. The key to these cases is furnished by accurate examinations of the urine. I have now a case in mind where a gentleman suffered with most violent and frequently recurring attacks of inflammation of the eyes for years. He, too, had headaches at times, which sometimes came before and sometimes after the conjunctivitis. He was treated chiefly for his eyes, and very little attention was paid to his headaches. I had his urine carefully examined, and it gave me the clue to the whole case; it was of high specific gravity, and full of uric acid and urates. There were no other symptoms save the attacks of eye inflammation that suggested gout. I put him on treatment for gout with this result, that, having had never less than four attacks of inflammation of the eye during the year, and often many more, he has now passed two years without an attack, and in addition to this the headaches have disappeared. This is only one case which it would be easy to multiply.

These remarks are made with the hope of helping the ophthalmologist in lines of work which he is the most competent to pursue.

OTOLOGY IN ITS RELATIONS TO GENERAL MEDICINE.

BY CLARENCE J. BLAKE, M.D.

Professor of Otology in Harvard University.

Somewhat more than twenty-five years ago, one of the first distinctly special practitioners in this country made a statement in open meeting to the effect, that general practitioners were to be considered as the rank and file, and specialists as the officers and staff of that army, whose business it is to fight, to conquer, and to limit the ravages of disease. It is needless to say that this proposition met with but little favor from his hearers and, notwithstanding the growth of specialism, and the division of the work done by the medical profession into parts having apparently often but very slight relationship to each other, it would meet with no more favor to-day. At the time when it was first made, specialism in medicine was a new, to many a dreaded, and to some an abhorrent thing. The general practice of medicine left the more minute investigation of many organs and their diseases untouched; bacteriology was not, and aseptic surgery had not yet come to point the shorter path to many a long sought goal, and cut the knot of many a medical problem.

With the experience of a quarter of a century, the simile between the medical profession and an army can be only justly used by comparing that army to a brotherhood, the members of which have each and all equal, though different functions, and if the general practitioner is to be classed with the rank and file, the specialist is to be regarded, not as in any way a superior officer, but as one of that rank and file sent out on special service; for, everywhere, the men who, with the foundation of the general study of medicine, and, still better, in addition, the practical study of general medicine as their base, go forward in any particular line of investigation, may be regarded as skirmishers sent in advance, whose duty it is, first of all, to observe, and second, to report back to the main body the result of their observations, and thus to indicate the lines on which that main body may advantageously proceed. It stands to reason, therefore, that the specialist, in whatever line his duty may take him, must be not only an observer, but in some way or other, and to a greater or less extent, a teacher; and the extent to which these func-

tions have been fulfilled, and these relationships of the interdependent parts of the medical community have been developed in the last twenty-five years, it is exceedingly interesting to observe.

The establishment of the nine special Societies which, in addition to the five others of more general purpose, make this august Association, are striking evidences of the fact that within the period mentioned, the growth of scientific medicine, and the enlargement of its field of observation, have so increased as to make it impossible for any one student to completely and adequately cover the whole ground; and we realize that it is, as always, the study of the infinitely little which has established the immeasurably great.

Thirty years ago, with few exceptions, there were not a sufficiently large number of medical men engaged in any special branch of research to form a Society. The first of the several special Societies forming the present Congress of American Physicians and Surgeons was founded in 1864, and the others followed in the order given in the circular of this Congress.

Buried deep beneath the surface, approachable only through a narrow and somewhat tortuous canal, containing within itself an example of almost every histological structure to be found within the human body, the human ear had long been a favorite study of those older anatomists, whose minute and painstaking investigations, and whose delicacy of research were in keeping with the work of their artist contemporaries.

As always, the anatomist lays the foundation stone; and to Meckel, Valsalva, Eustachius, and Corti, we are indebted for that knowledge which has made the study of diseases of the ear, both in itself, and in its relation to general medicine, one of the most fascinating of its kind. For not only does the inaccessibility of the organ require, on the one hand, trained manipulation in the surgical treatment of its diseases, but, on the other hand, the reflex relationship of the ear to other organs in the body, its visible and sometimes elucidative participation in other diseases, and its multiple office as an organ of hearing, as a peripheral organ of equilibration, and also as a supplemental organ of space perception, afford wide opportunities for that theoretical conjecture, which is the appetite of research, and the stimulus to scientific nutrition.

The mental processes which lead to effective results are always slow and concentrative, and in the brotherhood of scientific research some one mind advances a little beyond the others; some one thought reaching out seeks the support of facts, and makes suggestions which other minds may slowly follow; and precisely as the

study of the structure of the body long preceded the knowledge of its functions, and still further antedated the conclusions drawn from physiological investigation which laid the foundation of the art remedial and curative, so the simple device of a centrally perforated concave mirror which enabled the observer to stand behind his reflex light source lay unnoticed and practically unapplied, until at the end of fifty years it came into use in the hands of the clinician, and revolutionized, or rather, one might more properly say, made possible the study of the diseases of the ear in the living subject as they are studied and treated to-day; and the time has now passed when a celebrated aural surgeon saw patients only on bright days, and others used either a concentrating lens, or limited their manipulations to parts appreciable by touch.

In 1864, when in answer to a question from a visiting surgeon, "Why are you going abroad?" a young hospital house officer replied, "to study diseases of the ear," he was met with this statement, "All that you can do for the ear, you can do with a syringe." At that time there were in the United States but four medical men whose knowledge of diseases of the ear went beyond that indicated by the preceding remark, and these gentlemen were regarded by many in their profession as absurd in their claims as to the possibility of doing anything for the ear diseases beyond leaving them to the *vis medicatrix naturæ* with hope for the best results.

The study of diseases of the eye had at that time taken a recognized place as a branch of surgery and medicine requiring special education and special manipulative skill on the part of its practitioners, and departments in general hospitals, or special hospitals themselves for the treatment of diseases of the eye had already been established, in deference to the demands of public need, and were receiving the recognition necessary to their perpetuation in the form of public or private endowment. To these institutions there came, either as the result of a popular appreciation of the need of special treatment, or as the result of a popular association of ideas, patients suffering also from diseases of the ear; for such patients no provision was at first definitely made in the clinics of the general hospitals, or the out-patient departments of eye infirmaries, and they came under the care either of the general surgeon, or were, not uncommonly, transferred by him to the eye department, as one dealing with a branch of minute, if not minor surgery. The aural clinic, without special equipment of its own, came to be, therefore, in the beginning, by force of circumstances, and by lack of knowledge of its possibilities, an appendage to the department or hospital

devoted to the treatment of diseases of the eye, and it was not, in this country, until ophthalmic clinics had already been established, that a definite appointment as aural surgeon was made upon the staff of any of our hospitals, or that any instructor in this branch of medicine was appointed upon a faculty in a medical school. Even then, the specialty was slow in making its way to professional and public recognition, and the earlier records of investigation, as shown in Medical Journals, and the transactions of Societies, were those rather of physiological investigation and clinical observation than of advance along the lines of surgical procedure, in which this specialty has since taken its justly allotted place.

The foundation thus laid, however, was one which, once established, permitted the erection of a superstructure of minute definitions, and the history of the growth of Otology as a department of both medicine and surgery may be taken to include the following stages: *first*, the substructure of anatomical investigation, the study of the component parts of the machine, and their assembled relationships to each other; *second*, physiological research, the study of the machine in action, of the purpose of its individual components, and of their effective working relationship; *third*, as an outgrowth of these, the investigation of the pathologist into changes affected by diseases; *fourth*, and based upon these, the work of the clinician with reference to preventable cause and possible repair.

The earlier anatomical works contained elaborate treatises, and many accurate illustrations of the anatomy of the organ of hearing, and it is, perhaps, to its concealment within the body, as well as to the entrancing minuteness of its structure, that we owe the interest evoked by it in the earlier students of anatomy, and it is quite understandable that, but with little knowledge of acoustics, the study of a structure so complicated should have led to an intimate investigation of its parts, without the knowledge of their value, at a time when mysticism ruled, and the study of the black art constituted it a profession. It is not until the fifteenth century that we find the record of any accurate investigation with regard to that structure, in which Empedocles (400 B. C.) had discovered a snail-shaped body, which he considered as the real organ of hearing. The sixteenth century was especially rich among the Italians anatomists in minute and accurate investigation of this subject. Vesalius described the long process of the malleus, the Eustachian tube, the vestibule, and the semicircular canals. Ingrassia is probably entitled to the honor of the discovery of the stapes. Falopius described the tympanic cavity, the two fenestræ, and their communication with the vesti-

bule and the cochlea, and the communication of the mastoid cells with the tympanum, and gave his name to the canal through which the facial nerve passes to its point of exit below the ear. Eustachius described the intrinsic muscles, the tensor tympani, and the stapedius, gave a more exact description of that passage, leading from the middle ear to the throat, discovered by Vesalius, but called the Eustachian tube; while Casserius, of Venice, in the closing years of the sixteenth century, and the first of the seventeenth, gave a more complete description, than had been elsewhere previously published, of the sound-transmitting apparatus of the middle ear, and the sound-receiving portion of the labyrinth.

How recent is our more accurate information in regard to the structure of the ear is shown by the fact, that in the middle of the eighteenth century, the discoverer of the fluid of the labyrinth, Dominic Cotugno, won such a reputation by his work upon the internal ear, that he was called to the anatomical chair at Naples; while it was not until a century later, and within the memory of those who hear these words, that the first accurate description of the terminal sound-transmitting apparatus of the human ear was given by the Marchese Corti.

While specialization in medicine is no more definitely marked anywhere than in Otology, the investigation into the relation of diseases of the ear to the study of general medicine, is one which relieves it from a narrowness of interpretation, which would be inevitable were it confined merely to the exhibition of manual skill in the limited surgical field at its disposal. The long training, which alone makes the evidence afforded by inspection of the ear valuable, and which, therefore, sets the Otologist apart in his field as an observer, brings about the necessity of a relationship between the aurist and his brethren in general practice, and in other fields of special research, which would not pertain, were the information which he can afford, as the result of his acquired skill as a diagnostician, more readily within the knowledge of the body of the medical profession as a whole; a relationship, which it is needless to say, in addition to subserving a general, beneficent purpose, has its value in the encouragement of that interdependence, which is one of the great sources of the strength, as well as of the activity, of the medical profession.

In this sense, one of the gifts of Otology to general medicine may be said to be the interpretation of hidden things, nowhere more clearly shown than in the diseases of the ear occurring coincidently with the exanthemata of childhood, and in the review of the otologi-

cal subjects of common interest which makes the substance of this communication, it may very properly head the list.

That an acute congestion of the tympanic mucous membrane, resulting from closure of the Eustachian tube in the course of an acute coryza, may cause pain, general malaise, rise of temperature, and possibly nausea and vomiting in a young child, and that these symptoms may be relieved by the simple procedure of opening the Eustachian tube, is well known; but that these symptoms, without pain, with excessive temperature, and evidences pointing to profound cerebral disturbance, coma, and convulsions, may be due solely to the same cause, and entirely relieved by the same remedies, or by a simple puncture of the drumhead by means of a paracentesis needle, is not as well known, and it is not until recently that we have come in the profession as a whole to realize the full importance of the stand taken by the late Dr. Edward H. Clark, of Boston, and quoted with approval by no less an authority than Von Troelsch, in these words, "So necessary is a careful attention to the ear during the course of an acute exanthemata, that every physician who treats such a case without careful attention to the organ of hearing, must be denominated an unscrupulous practitioner."*

The participation of the ear also in diseases of the pleural cavity in childhood, its implication during the process of dentition, and the serious general effect which the disturbance of so vascular and so sensitive a structure in intimate relationship with the brain may have as a complicating factor in some already serious general condition, make the investigation of the ear often a matter of grave importance; while, on the other hand, the demonstration of the fact that the ear is in no way concerned, and that its inspection gives the purely negative evidence of a healthly condition, may often help, by eliminating one possible factor of disorder, to the solution of a complicated problem in diagnosis, for it is especially in children, on account of the intimate reflex relationships of the ear, that that organ comes most frequently into question as a possible causative or participative agent in other diseases.

"The great vascularity of the canal, the drum-head, and the middle ear in children favors the rapid course of an infective inflammatory process, and, in a child suffering from scarlet fever or measles, with other sufficient cause for rise of temperature and complaint of pain, a discharge from the ear is often, in default of the

* Perforation of the Membrana Tympani; its causes and treatment. American Journal of the Medical Sciences, January, 1858.

aural inspection which should be considered imperatively a part of the examination of all such cases, the first evidence of an implication of the ear.

The external auditory canal in the young child is principally cartilaginous, the bony canal, which in the adult forms the inner half, being formed partly by development of the osseous tympanic ring, and partly by the projection of the mastoid cells outward, forming the posterior wall. The fact that deficiency in bony development is not uncommon, and that the vascularity and delicacy of the soft tissues favor inflammatory invasion of the surrounding parts, emphasizes the importance of keeping a strict watch upon all cases of diseases of the external and middle ear in children, a not uncommon complication to be borne in mind, being the simple post aural abscess, which, if not speedily treated surgically, results sometimes in extensive denudation of bone, superficial caries, and still more serious consequences.

The most frequent diseases of the ear in childhood are those occurring in the middle ear, either secondarily as the result of extension of inflammation from the external ear, or from the naso-pharynx through the Eustachian tube, the latter by far the more common channel for the invasion of the middle ear, and the primary mechanical cause being usually either the simple congestion and swelling of the mucous membrane of the nose and naso-pharynx, such as may occur in the course of an ordinary head cold, the presence of the so-called adenoid growths in the naso-pharynx, or the inflammation of the mucous membrane of this cavity, the Eustachian tube, and middle ear, incident to the course of the exanthemata.

In the first and second instance, the middle ear is affected primarily as the result of the closure of the Eustachian tube, either by the swelling of its lining-membrane or by the pressure of an adenoid growth, the results being interference with the ventilation of the ear and its blood supply, and a congestion of the middle ear, which in coryza is usually more acute than in the acute cases where the pressure of the adenoid growth produces a static congestion. In the 'earache of childhood,' which is most commonly the result of a simple acute inflammation of the middle ear, attention must be directed, not only to the organ specially affected, but to the nose and naso-pharynx and to the general condition of the child,—a faulty diet or faulty habits of life being often found to be the predisposing causes; while, in the cases of adenoid growths, early surgical treatment, thoroughly carried out, is the best radical measure. One of several objections to the partial and frequently repeated

operation without ether for the removal of adenoids is, that, while the central growth may be thus disposed of, the region of the Eustachian tube, which needs especially careful manipulation, is left comparatively untouched, and, while there may be satisfactory evidence of the establishment of nasal breathing, the passage of air through the Eustachian tubes to the middle ears is hindered by the presence of the remaining lateral portion of the adenoid growth; therefore, with reference to relief of the aural symptoms, the complete operation, under anaesthesia, permitting thorough and careful manipulation of the tubal region, is preferable.

In the child the vascular anastomoses are large and numerous, and the divisions of the temporal bone do not assume their relationship of complete ossification until after puberty; the mastoid process, which subsequently forms the posterior wall of the osseous canal, and presents in its interior a mass of diploetic and pneumatic cells, the latter communicating with the middle-ear cavity, is represented in the young child by the mastoid antrum, indirect communication with the middle ear, and immediately beneath the thin plate of bone, later known as the tegmen mastoideum, which forms the boundary between this and the cranial cavity, while the sutura petroso-squamosa permits direct communication, through membranous connections, largely supplied with blood-vessels, between the lining-membrane of the tympanum and the meninges.

The importance of frequent objective examination of the ears during the course, especially in the acute stage, of scarlet fever and measles, is emphasized by the fact already stated, that the middle-ear disease, occurring as a complication of these affections, usually runs a rapidly destructive course, and by the further fact that aural symptoms, other than objective ones, unless unusually severe, are apt to be lost sight of in the consideration of the general condition of the child,* while the importance of bacteriological examination is nowhere better illustrated than by the fact that Klebs-Lœffler bacillus has been found in a discharging ear long after it had ceased to be found in the throat."

Inasmuch as the ear is the channel through which a large part of the educational material is supplied to the brain during adolescence, the importance of testing the hearing and examining the ears of school children is a subject which should command both the interest and influence of the profession at large.

*The relation of an Aural Service to the needs of a General Hospital for children. Clarence J. Blake; Medical and Surgical Report of the Children's Hospital. Boston, 1895.

Everywhere the doctor, as is incumbent upon him from the high trust which he holds, and in the acknowledgment of the privilege which he has of being a doctor, is called upon more and more to exercise those duties of citizenship which have to deal with the questions of conservation to its greatest usefulness of the one piece of personal property with which each individual in the community is possessed from his birth, and the questions of public hygiene, of the perpetuation of health, and the prevention of disease, of the encouragement of healthy activity, and the utilization, as well as the protection, of the waste humanity which is a public charge, are making justifiably larger and more imperative demands upon the time and thought of the citizen doctor.

The establishment of medical boards of supervision in public schools is one of the important opportunities afforded the medical specialist, for not only should the children be examined with reference to contagious diseases, for the safety of those as yet uncontaminated, but they should be examined also with reference to their ability to avail themselves of the educational opportunities afforded. The truth of this proposition will be best appreciated by those whose study of school children in respect to defects of sight and hearing will have shown them the unexpectedly large number of such children justly entitled to compensatory advantages.

"The generally received opinion that diminution of hearing in children in consequence of disease is rare, is a mistaken one; indeed, in some localities, the cases of disease of the ear exceed in number the cases of disease of the eye, and, moreover, they are apparently on the increase; the steadily increasing demands upon the mental capacity, accompanying the advances of the times, bring the defects of hearing more prominently forward, because they show themselves to be a decided hindrance to the better education of the child. The results upon its later mental development of a marked diminution of hearing in a child are, unless compensated for by other instruction, decided and permanent, affecting the understanding, the character, the self confidence, and, at a later period, the ability of self-support; mental tools, the possession of which is valuable, and the want of which can never adequately be supplied."* In this view, it is certainly a matter of importance that more attention should be directed to the detection of partial deafness in school children, in order that proper remedial efforts may be made, or in default thereof, proper compensatory advantages afforded.

*Franciska Schaeling. Thorn, 1872. Beiträge zu einer richtigen, leiblichen und geistigen Erziehung gehörkranker Kinder.

Very nearly twenty-five per cent. of the patients attending our aural clinics are children under fourteen years of age; of this number fifty per cent. are the subject of suppurative inflammation of the middle ear, and of this number ten per cent. or more owe their origin to the exanthemata of childhood, while of the cases of deaf mutism throughout the United States, twenty-seven per cent. have been the result of suppurative middle-ear disease in early childhood, and it is probable that the more thorough investigation, and the systematic examination of the ears of children in our deaf mute schools, which it is to be hoped will sometime be the rule, will show a still larger percentage of these cases.

Indeed, one of the duties of the American Otological Society, as representing to the profession at large its special line of work, is to urge that systematic examination of the ears of children in our deaf mute institutions, which shall, in addition to throwing the needed light upon the etiology of this deficiency, give the individual opportunities for improvement not otherwise obtainable.

It is equally incumbent upon the members of the Society individually to give to such examinations their personal attention, and to this end, the appointment of a competent aurist as a part of the Staff of every considerable deaf mute institution in this country would be an advantage; for although the proportion of children in such institutions actually suffering from suppurative disease of the middle ear is probably not more than five per cent., the number of cases of partial hearing for some portion or other of the musical scale or of vowel tone perception is much larger than was formerly supposed, and in the schools in which the articulate method of instruction is pursued, the utilization, and possibly, the encouragement of this tone-hearing becomes an important factor not only in the patient's ability to intellectually interpret the substitute for sounds which is presented to him, but puts him on a better plane of communication with his fellow men, by helping him to achieve a better articulation himself.

The surgery of the ear differs from special surgery of other portions of the body, in the important respect of the wide range of manipulative skill required, from an exploratory tympanotomy done under reflected light, through a tube an inch long and less than half an inch in diameter, under the most exacting aseptic precautions, on the one hand; to an operation in a pus cavity, including the thorough evacuation of the cellular structure of the mastoid process of the temporal bone, with the possible extension of the operative field to the cranial cavity, for the purpose of opening the

lateral sinus, or evacuating a brain abscess, on the other hand: is certainly a field wide enough to awaken interest, and fruitful enough to stimulate endeavor.

The progress which has been made in what may be called the minor operative procedures in ear diseases has come about as the result of a more intimate study of the structure of the ear on the part of the clinician, and a better adaptation of instruments to the end desired, and in this latter respect, as in many others, the aural specialist owes much to suggestions obtained from parallel lines of research; for the instruments necessary for the surgery of the middle ear are quite as delicate as those demanded for operations upon the eye, and the mechanical skill of the dentist has contributed much to the facility with which surgeons now treat diseases of bone.

The complicated construction of the temporal bone, and the number of important structures in contact with, or situated in very close relation to, the cavity of the middle ear, make the minute study of these relationships absolutely necessary as a preliminary to the adequate surgical treatment of its diseases, and what might well be made a text-book on the surgery and the surgical anatomy of the temporal bone in view of the later contributions of this subject, yet remains to be written. Given in the adult a suppurative process in that bony cavity known as the tympanum, bounded by its outer wall of membrane which has been already punctured for the liberation of the contained and rapidly secreting pus, we have a possibility of the extension of the inflammatory process from the middle ear into the cavity of the mastoid bone, and thence of the passage of pus through some thin point in the wall of the mastoid cavity downward into the tissues of the neck, or inward into the cranial cavity, and there may be as the ultimate result of an inflammation starting in a cavity less than half an inch in its longest, and no more than a thirty-second of an inch in its shortest diameter, a meningitis, a thrombosis of the lateral sinus, or an abscess of the brain. Professor Politzer, in one of his courses of lectures, was accustomed, holding a temporal bone by its styloid process, and turning it slowly before the class, to say, "Gentlemen, the temporal bone has four sides; the outside is bounded by life, from which there comes through the opening of the external auditory canal one form of our appreciation of what life means; on the other three sides, this bone is bounded by death." Dramatic as this statement was, it had the desired effect of a text, in fixing the attention of the student, and it had, moreover, the merit of being, on further consideration, and

with a deeper knowledge of the subject, strictly true; for it is only necessary to place side by side the earlier records of autopsies, which revealed an abscess of the brain, and the records of any considerable aural clinic to-day, with its list of successful operations upon the mastoid, the lateral sinus and the brain, and to read the growing literature on the subject of otitic brain abscess, to realize the gift in this respect of aural surgery to the profession, and the reason which the general surgeon has for respecting this special field; a gift which is, however, no more than an acknowledgment of favors received, for the whole success of the specialist in the surgery of the temporal bone is the fruit of the application of broad general surgical rules, together with special anatomical knowledge, to the solution of the critical problem; while the surgery of the middle ear in cases of suppurative disease is again that application of general surgical rules reduced to the dimensions of the cavity with which it has to deal.

The surgery of a suppurative process within the temporal bone, which, beginning in the middle ear, has implicated the mastoid process and threatens contiguous structures, has to take into consideration, not merely the effort to save life, but also to conserve, so far as may be possible, the hearing power, and to leave undisturbed the equilibrating function of the ear; but it has also to take into consideration the possibility of injury to important structures lying in minutely close relationship to the necessary operative field.

Under these circumstances it is a tenable proposition that no aural surgeon should undertake an operation upon the mastoid in a case of suppurative implication of that cavity, without being prepared by his mental and material equipment to enlarge his operative field to any extent demanded, or without having, if he does not possess it himself, the necessary surgical assistance and counsel at hand.

The fact that it is easier for the aurist to learn to open the cranial cavity, and to operate upon the lateral sinus or the brain, than for the general surgeon to acquaint himself with the technical procedures of operation within the temporal bone and middle ear, is an argument in favor of leaving the subject of the intra-cranial complications of suppurative middle-ear disease where it now largely stands, in the hands of the special practitioner.

Of the diseases of the ear which come under the consideration of the general practitioner, and which do not menace life, the first in the list is the so-called chronic catarrhal inflammation of the middle

ear, which makes in the temperate zone about thirty per cent. of all the material ultimately referred to the aural specialist. Under the broad title of chronic non-suppurative diseases of the middle ear, there lie hidden a series of changes in the soft tissues of the sound-transmitting apparatus, which are still the subject of interested study and investigation; and one of the many fields of research open to the student of the future in Otology is the further acquired differentiation of those alterations in structure, the result of disease, which interfere with the transmission of sound, and the etiology of which is often to be traced to a remote source. As an example of this, may be taken the peculiar, and often puzzling, cases of variable hearing, occurring in young women, who ultimately become very deaf to all sounds aerially conveyed. The great variations, occurring as they do in girls soon after puberty, or in young women who were the subjects of considerable nervous and emotional strain, led, without other ascertainable cause, to the conclusion that these variations were purely of neural origin, and being merely symptomatic, were to be discharged, or to be dealt with solely through attention to the general condition. A special study of these cases, however, through the aural speculum, showed, under conditions of the greatest hearing impairment in many of them, a localized congestion of the tympanic mucous membrane, especially of the niche of the oval window around the stapes. This peculiar blush was found most commonly, periodically in connection with the disturbances of the menstrual functions, or with other evidences of pelvic disorder, and with the assistance of the gynæcologist, it was found, in the great majority of cases, that there was either malposition of the uterus, erosion of its neck, or atresia of its cervical canal, and that the remedying of these defects had a very material and beneficial influence upon the localized circulatory disturbance, and accompanying tissue change in so important a portion of the middle ear as is the inner end of the sound-transmitting chain of bones.

Another example of the interdependence of the aurist and the general practitioner is shown in the cases of chronic non-suppurative middle-ear disease in which the deleterious changes in the lining membrane of the tympanic cavity are furthered by general nervous overstrain, overtire, and the coincident train of disturbances of nutrition. In these cases, the local treatment of the ear is futile, or of but little and temporary benefit without careful attention given to general hygiene, and to a consideration of the condition of environment of the patient, climatic or otherwise. The depend-

ence upon local treatment alone in such cases is sometimes mischievous in its results, and at least fails of the benefit which might accrue from a broader view of the situation, and emphasizes the importance of a consultation between the aurist and the physician, who as the family adviser has cognizance of the conditions which may have an important bearing upon the etiology and progress of the case in question.

The first tendency in specialism is to lay stress upon the special character of the investigation to be followed, and to emphasize its individuality, and with the broadening of the study, its relationship to, and dependence upon general scientific research, becomes more and more evident. Specialized specialism ceases to exist, in proportion as it separates itself, and grows and broadens only as it keeps up its relationship with the main body; and here again the military simile may be employed, for the specialist, who as a skirmisher exploring unknown country, cuts himself off from the main body which is his support, and to which he owes his allegiance, and who seeks to exist to himself alone, fails of that usefulness in the line of duty, which is the invariable price of any existence whatever.

One of the most striking examples of elucidative work in Otology is that which has had to do with the definition and explanation of the curious complex of symptoms of which vertigo is the most marked and incapacitating manifestation.

With the recognition of the ear as a peripheral organ of equilibration, and with increased knowledge of its reflex relationship to the sympathetic nervous system, the better definition of its blood supply, and the differentiation of its vaso-motor tracts, came an explanation of much that had been vague and mystifying in those cases of vertigo of sudden onset, which had formerly been referred either to abnormalities in the circulation of the brain, or to disturbances of the digestive apparatus, as their amenable cause; and the advances made in the study of the physiology of the sound-transmitting apparatus, and in the application of surgical rules to the treatment of diseases of the middle ear, has brought to our knowledge the possible advantage of establishing still another differentiation, that of *aural*, as distinguished from *auditory* vertigo.

It is now a recognized fact, that an effusion or hæmorrhage occurring in the labyrinth may affect the hearing or the balancing power, or both, of the individual, to a greater or less degree, according to its location and extent, and that the symptoms, so far as equilibration is concerned, may gradually disappear, to be reawakened at a later period by general conditions which induce a

suspense of vaso-motor inhibition, and thereby, a secondary irritation of the terminal nerve apparatus. It is further established, that a fixation of the sound-transmitting apparatus of the middle ear, by doing away with, or decreasing, the function of one of the outlets from the labyrinth for pressure exerted by dilatation of the intra-labyrinthine vessels, favors disturbance of the nervous end apparatus by a lesser degree of circulatory pressure than would be possible were the elasticity of the membranes of the round and oval windows, and the mobility of the ossicular chain unimpaired.

The records of aural clinics show an increasing observation of cases of suppurative disease of the middle ear, in which pressure upon the stapes as the result of a new growth, or of epidermal exfoliation, causes a series of symptoms very closely resembling those of the so-called Ménières complex, and in which vertigo plays a prominent and disturbing part. These cases are almost invariably relieved by the removal of the morbid growths or accumulations, and the consequent release of the labyrinth from extrinsic mechanical pressure, and constitute the class of what may therefore be called the mechanical or aural vertigoes. For purposes of distinction, the first series of cases just cited may be termed auditory or labyrinthine vertigo, and the second class may be considered as lying between these two extremes. Beyond this grosser differentiation, it is possible to go into minute definitions as to immediate or reflex cause and effect, and to follow the subject into the domain of the neurologist, before it shall in any degree have received the attention in investigation which its importance demands; while the question of intra-labyrinthine lesions as an accompaniment of diseases of the kidneys, of the digestive apparatus, of the pelvic organs in women, and of the constitutional diseases, of which syphilis stands at the head of the list in the number of cases of labyrinth implication, and of diseases of the internal ear in children, present problems towards the solution of which the general practitioner and the otologist may well take counsel together.

There is one other subject which should command the attention both of the aurist and the general practitioner, and that is what may be called the "fatigue of deafness," a common and often unestimated factor in the causation and persistence of neurasthenia, and one imposing upon sometimes feeble shoulders a burden which it becomes us to lighten, if we cannot lift.

It may be taken as an accepted fact, among other evidences of the bounty of nature, as set forth in the construction of this temple

of the body, that those of us who have normal ears start in life with double the amount of hearing absolutely necessary for the ordinary purposes of social communion, and it is therefore possible to lose one-half of one's hearing power before becoming conscious of the loss. Under these conditions, where the daily ordinary use of the hearing is regarded as the standard of perfection, it is easily understandable, that a chronic progressive disease impairing the hearing may become fairly established before attention is turned to the necessity of interference, with a view to prevention and repair, and it is therefore not unusual to find in the majority of the chronic progressive diseases of which the slow impairment of hearing is the important symptom, that they have by the time they come into the hands of the aurist long passed the possibility of prevention, and have established a condition which can be in only a moderate degree repaired. The apparent hopelessness of many of these cases, the impossibility of effecting by the treatment more than a slight improvement, should be no deterrent to the honest and strenuous effort to ameliorate the condition of cases of this class, and it is in many of them that the general practitioner, the family physician, and the specialist, can best work hand in hand; for the deleteriously causative and influencing factors in the general condition in these cases are so many, and the progress toward improvement so slow, that the local treatment may often be advisedly limited to that which the patient can himself effect under the observation of his physician, with occasional examination and suggestion from the specialist, and there is probably no class of cases, although coming under the care of the aurist, which is so likely to become the subject of what may be termed over-treatment, either surgical or medical, as the chronic non-suppurative diseases of the middle ear. It is especially in connection with these cases of slowly progressive impairment of hearing that the fatigue of deafness manifests itself. Few intelligent observers outside of the very deaf themselves, or of those who have to deal much with persons so afflicted, can appreciate the profound exhaustion resulting from the effort to compensate for a deficiency in this particular line of communication with the outer world, in the person whose perception of that mode of motion to which we give the name of sound was once made without appreciable effort, and who has, under conditions of impaired hearing, first of all to make an effort to hear, and in default of hearing, an effort to appreciate vocal utterances by watching the motion of the lips of the speaker, and finally in default, either through lack of perceptive power, or through ability only to catch consonant sounds

which are formed in front of the mouth, to solve the puzzle of the spoken sentence by filling in the missing consonant sounds, those imperfectly heard, or inadequately seen, from the appreciated context of the sentence; so that where once understanding came without effort, three distinct and appreciable brain efforts are required; the first, to hear; the second, to see; and the third, to understand. In our estimate of the burdens of life, the consideration of which belongs especially to the ministry of the medical profession, we should, I think, all of us endeavor to estimate more justly as scientific observers, more kindly, perhaps, as fellow creatures, the nervous strain, the restrictive limit to useful expenditure of energy, and the demand for compensatory consideration for the pitiably deaf.

It has been impossible within the compass of this address to do more than touch upon some of the points which make the relationship of Otology to General Medicine; a relationship, which it becomes the practitioners of both to conserve and strengthen, with the purpose of keeping the specialist from becoming narrow, and of giving the general practitioner opportunities for gaining something more than a superficial knowledge of this special line of work.

To this end, the further establishment of obligatory courses in the medical schools, with clinical lectures and instruction in methods of diagnosis and treatment, with clinical conferences, and a practical examination of the student at the close of the course, are among the suggestions to be made; while for the graduate student, in this country, as is now the case abroad, systematic courses, including opportunities for the study of the structure and development of the ear, its anatomy, its bacteriology and the pathology of its diseases, in addition to clinical instruction, should be afforded.

The experience of teachers in this department of medical instruction shows that more time is required to give a student the knowledge of diagnosis adequate to his future uses as a general practitioner than is required in almost any other branch of special medical study.

The inaccessibility of the deeper and more vulnerable parts of the ear, and the minuteness of the objective field, with the changes in the diagnostic picture presented during the ordinary course of any of the more important diseases and the variations incident to complications which may occur, make accurate determination of the true condition, except to a trained observer, often a matter of great difficulty.

The inducement which led the medical student of thirty years

ago to take up the study of diseases of the ear because it presented a promising domain for original research is as true to-day, with its widened horizon, as it was then, and grows with the growing appreciation on the part of the Otologist that his study, in its demand for better preliminary education in acoustics, better knowledge of pathology, with its suggestions for future use, better knowledge of bacteriology in its relation to diseases of the ear, and better knowledge of the general diseases in which the ear may be implicated, is one which affords such great opportunities for scientific investigation and helpful usefulness as to make it worthy of the earnest and unwearying devotion of a lifetime.

INTERNAL SECRETIONS CONSIDERED IN THEIR PHYSIOLOGICAL, PATHOLOGICAL AND CLINICAL ASPECTS.

Physiology of Internal Secretions.

BY WILLIAM H. HOWELL, M.D.

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We owe the term "internal secretion" to Brown-Séquard,* by whom it was first used in published communications dating from 1891. The essential idea conveyed by the expression, however, is not new, as it has been stated more or less clearly by many previous writers in their speculations upon the probable functions of the so-called ductless or vascular glands. It had long been recognized that these glands possess no excretory ducts, and that, therefore, whatever secretion they may produce probably enters the blood either directly or by way of the lymph. Haller† is credited with stating this view with regard to the thyroid as early as 1776, and according to Pettit‡ a similar view was advanced by Schmidt in 1785 with regard to the suprarenals. Toward the middle of the present century this belief was generally accepted for such glands as the thyroid, suprarenal, thymus, hypophysis cerebri and spleen, but as early as 1869 Brown-Séquard seems to have suggested the view that all glands, whether possessed of excretory ducts or not, give off something to the blood that is of importance in the general nutrition of the organism. From 1889 his ideas took definite shape in numerous publications§ upon the physiological effects of injections of extracts of the testis. At first he did not use the term internal secretion, and seems to have held the view, so far as the testis is concerned, that the material furnished to the blood is absorbed

* Brown-Séquard and d'Arsonval: Comptes rendus de la Société de Biologie, 1891.

† Jones in Todd's Cyclopædia of Anatomy and Physiology: Article on Thyroid Gland.

‡ Pettit: Recherches sur les capsules surrénales, 1896—Paris. Thèse de la Faculté des Sciences.

§ Brown-Séquard: Archives de Physiologie normale et pathologique, 1889–92.

from the external secretions and is normally carried off in part in this secretion.

During this same period the brilliant results of the experiments made upon the thyroid glands and the pancreas were forcing themselves upon the attention of physiologists, and these results, together with his own experiments upon the extracts of testis and ovary, and his previously expressed belief as to the possible effect exercised by all glands upon the composition of the blood, seem to have led

Note.

Professor Davenport calls attention in Science, Aug. 6, 1897, to the fact that Claude Bernard makes use of this term in his "Rapport sur les progrès et la marche de la physiologie générale en France," 1867, and moreover that he makes a clear distinction between internal secretions and external secretions in the sense accepted at the present day. The term internal secretion was not, however, generally adopted in physiological literature until Brown-Sequard gave it currency in his numerous publications.

W. H. H.

muscle, nerve and connective tissue.

So far as I am aware, there is no authorized definition of the term internal secretion, but if we adhere closely to the facts in the case, the expression may be interpreted to mean certain products that are elaborated by gland cells from material furnished by the blood, which are afterwards passed back to the blood or lymph stream to subserve some function in general or special nutrition. From the standpoint of mechanism of secretion a useful distinction has been drawn between these internal secretions and secretions of the usual kind, or external secretions. The latter are in all typical cases poured out upon a free epithelial surface that communicates with the exterior, while the internal secretions are discharged upon the closed endothelial surfaces of the blood and lymph vessels.

The definition given by Brown-Séquard, as we have seen, attributed internal secretions to all tissues. As a part of this general

INTERNAL SECRETIONS CONSIDERED IN THEIR PHYSIOLOGICAL, PATHOLOGICAL AND CLINICAL ASPECTS.

as the thyroid, suprarenal, thymus, hypophysis cerebri and spleen, but as early as 1869 Brown-Séquard seems to have suggested the view that all glands, whether possessed of excretory ducts or not, give off something to the blood that is of importance in the general nutrition of the organism. From 1889 his ideas took definite shape in numerous publications§ upon the physiological effects of injections of extracts of the testis. At first he did not use the term internal secretion, and seems to have held the view, so far as the testis is concerned, that the material furnished to the blood is absorbed

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from the external secretions and is normally carried off in part in this secretion.

During this same period the brilliant results of the experiments made upon the thyroid glands and the pancreas were forcing themselves upon the attention of physiologists, and these results, together with his own experiments upon the extracts of testis and ovary, and his previously expressed belief as to the possible effect exercised by all glands upon the composition of the blood, seem to have led Brown-Séquard to the generalization expressed in the happy term "internal secretion." The term as used by him was not restricted to the glandular tissues alone, but was meant to signify that all the tissues in the body furnish something of special importance to the blood—that, in fact, every act of nutrition is accompanied by an internal secretion. This broadening of the term to apply to all the tissues is logical, perhaps, but it must be admitted, I think, that so far as our actual knowledge goes it is not justifiable. The evidence derived from experimental investigations and clinical observations indicate that many, although not all, of the glandular tissues of the body as one result of their normal metabolism add something to the blood or affect its composition in some way, and that this activity is either essential or helpful to the maintenance of the normal functions of the organism. In this list we can place such glands as the liver, pancreas, thyroid and parathyroid bodies, suprarenal bodies, hypophysis cerebri, and probably the ovary, testis, thymus and spleen. But I know of no observations that force us to entertain a similar belief with regard to the non-glandular tissues, such as muscle, nerve and connective tissue.

So far as I am aware, there is no authorized definition of the term internal secretion, but if we adhere closely to the facts in the case, the expression may be interpreted to mean certain products that are elaborated by gland cells from material furnished by the blood, which are afterwards passed back to the blood or lymph stream to subserve some function in general or special nutrition. From the standpoint of mechanism of secretion a useful distinction has been drawn between these internal secretions and secretions of the usual kind, or external secretions. The latter are in all typical cases poured out upon a free epithelial surface that communicates with the exterior, while the internal secretions are discharged upon the closed endothelial surfaces of the blood and lymph vessels.

The definition given by Brown-Séquard, as we have seen, attributed internal secretions to all tissues. As a part of this general

conception he was led also to restate what appears to have been a dream of the older physicians, namely, the view that all animal tissues might and ought to be employed in special cases as means of medical treatment, extracts of each organ or tissue being recommended for the particular disease supposed to be due to disturbance of function in the corresponding tissue. This general conclusion seems to have been a wide induction upon the basis of the incomplete facts known at that time with regard to the therapeutical use of extracts of thyroid and testis. It was not entirely justified by actual experience then or now, but the attractive possibilities it presents have doubtless been the cause of much of the general interest manifested in the subject of internal secretions. A new field, hitherto almost unexplored and full of promise for the discovery of medical specifics, seemed to be opened to the medical profession, and much activity has been exhibited in exploiting the possibilities of this kind of therapeutical treatment for which the names *opotherapeutics, organotherapeutics* and *histotherapeutics* have already been suggested.

It must be borne in mind, however, that these promises are in large part premature. The one clearly successful method of treatment by animal tissues is the use of thyroid extracts, and the demonstration of the value of this method was the result of rigorous scientific work extending over more than a decade, and was obtained quite independently of the generalization announced by Brown-Séquard. It seems perfectly certain that whatever else of value may come out of the therapeutical application of tissue extracts must also be established by intelligent scientific research, on the side of experimental as well as clinical medicine, and not by indiscriminate and over-anxious attempts to secure immediate results.

It is my purpose to-day to call your attention briefly to some of the important results obtained by experimental physiology that tend to prove the existence of internal secretions in a number of glandular organs. The main interest to the physiologist lies, perhaps, in the light this work has thrown upon the functions of the blood-glands, or ductless glands, especially the thyroid, suprarenals, hypophysis cerebri, thymus and spleen. Forty years ago the physiology of these bodies was not only unknown, but was beyond the reach of intelligent hypotheses. Within recent years facts have accumulated, especially with regard to the thyroid and suprarenals, that give us a new standpoint from which to view their physiology—a standpoint also from which experimental investigations may be

planned with reasonable hope of abundant success in the future. I shall not attempt an historical review of recent work in this subject, as this has been given already in numerous general addresses and special papers.* I desire only to emphasize what seems to be the outcome of the physiological work that has been done in the last twelve or thirteen years, and to explain briefly the character of the work now in progress.

If we include under the term "thyroid tissue" not only the thyroid body itself, but also the accessory thyroids and the neighboring parathyroids, it has been shown beyond reasonable doubt that complete removal of this tissue in man and the related mammals is followed, as a rule, by serious disturbances of nutrition that are immediately or ultimately fatal to the animal. Moreover, in these cases the reintroduction of thyroid material into the body, whether this introduction be made by grafting the tissue, by subcutaneous or intravascular injections, or by absorption from the alimentary canal, results in an amelioration or even entire removal of the symptoms of malnutrition. The physiologists recall with pleasure that these two fundamental facts were first discovered as the result of experimental work in physiology. The effects of complete thyroidectomy were first described by Schiff† in 1856, and the therapeutical use of thyroid tissue arose naturally from the grafting experiments of Schiff‡ in 1884 and the subsequent experiments of Vassale§ and of Gley‖ upon injections of thyroid extracts. The brilliant results that have followed the use of thyroid tissue in man in cases of myxœdema, goître, etc., are too well known now to require more than a passing reference.

It follows as a logical conclusion from the successful effects attending its therapeutical use, as well as from the evil effects of its destruction or removal, that the thyroid tissue produces, normally, something that is in some way essential to the nutrition of the body. What that something is has been revealed partially by the beautiful chemical and clinical researches of Baumann and

*See especially Abelous: *Revue général des Sciences*, May 15, 1893. Schäfer: Address in Physiology; Annual Meeting of the British Med. Assoc., London, 1895. Meltzer: On Thyroid Therapy; *New York Med. Jour.*, May 25, 1895.

† Schiff: Untersuchungen über die Zuckerbildung in der Leber, etc., Würzburg, 1859.

‡ Schiff: Revue médicale de la Suisse romande, 1884.

§ Vassale: Rivista sperimentale di freniatria, etc., Vol. XVI.; also Centralblatt f. d. Med. Wiss., 1891.

‖ Gley: Comptes rendus de la Soc. de Biol., 1891.

Roos. Baumann* has succeeded in isolating a substance, thyroiodin, or iodothyrin, as it has been named more recently, which, according to the experiments of Roos,† preserves the beneficial effects of thyroid tissue.

The chemical characteristics of this compound will doubtless be presented in Professor Chittenden's paper. It has proved to be a very stable compound, unaffected by boiling, by strong acids and by gastric digestion, and this fact may be taken as a complete disproof of a former view to the effect that the action exerted upon the body by thyroid tissue is due to the presence of special enzymes or ferments. The fact that extracts of thyroid tissue or iodothyrin when absorbed into the blood ameliorate or remove the evil effects resulting from loss of function of the thyroid, seems to prove at once that the normal function of thyroid tissues is not merely to excrete poisonous material from the blood after the manner of the kidneys. It indicates, on the contrary, that these tissues act normally by giving off a material to the blood that in some way affects favorably the nutrition of all or a part of the tissues of the body. In other words, the thyroid tissues form a true internal secretion. Histological research indicates that, so far as the thyroid bodies proper are concerned, this secretion is contained in the so-called colloidal material that accumulates in the interior of the vesicles, and that the mechanism of secretion consists in a rupture of the walls of the vesicles at some point whereby the contents are discharged into the surrounding lymph spaces.‡

The most important fact that remains to be discovered is the manner of action of this secretion upon the tissues of the body. At present we can only speculate upon the answer to this problem. More experimental work is required before a definite solution can be reached. To account for the action of the thyroid secretion two main hypotheses have been proposed. According to one hypothesis the function of the secretion is antitoxic. In some way it antagonizes an unknown toxic substance supposed to be formed in the body in the course of normal metabolism. When the thyroid tissues are removed this poisonous material, being imperfectly excreted, accumulates in the blood and produces the fatal symptoms of thyroidectomy by a process of auto-intoxication. The

* Baumann: Zeitschrift für physiolog. Chemie, Bd. XXI., 1896; also Bd. XXII.

† Roos: Ibid, Bd. XXII.

‡ Biondi: Berliner Klinische Wochenschrift, 1888. Langendorff: Archiv. für Physiologie, 1889, Suppl. Bd. Schmid: Archiv. für mik. Anatomie, 1896.

other hypothesis assumes that the secretion of the thyroid acts normally by promoting or regulating the metabolism of other parts of the body, particularly, perhaps, of the nervous tissues. We might designate this as the trophic or neuro-trophic hypothesis. It is less specific than the antitoxic hypothesis, and therefore, perhaps, less objectionable in the present incomplete state of our knowledge ; but as no decisive, or even probable, proof can be given for either view, it seems unnecessary to criticise the various facts brought forward in support of one or the other of them. The two great facts to be explained are : first, that the complete removal of the thyroid tissues brings on a condition of malnutrition that seems to affect especially the central nervous system; and, second, that injection or ingestion of thyroid extracts while the animal is in this condition restores its metabolism more or less completely to the normal state. While both of these facts are explicable in terms of either of the hypotheses mentioned, the trophic theory does not involve the somewhat strained assumption of an unknown toxic product of metabolism that can not be got rid of completely by the usual methods of excretion.

A very interesting phase of thyroid physiology that has recently come to the front is the nature of the functional relationship between parathyroid tissue and thyroid tissue proper, such as is found in the thyroid body and the accessory thyroids. The parathyroids seem to occur in all mammalia. According to a recent description by Kohn* there is always one of these bodies on each side attached to the external or posterior surface of the lateral lobes of the thyroid, while in some animals, *e. g.*, the dog, cat and rabbit, there is an additional one on each side, imbedded in the substance of the thyroid lobes. Histologically the structure of these small bodies bears no resemblance to that of the thyroid. They possess the general appearance of embryological tissue, and have, therefore, been regarded usually as an immature form of thyroid tissue, which, under the stimulus of increased functional activity, is capable of developing into normal thyroid structure. Satisfactory evidence is lacking that such a transformation does actually take place under the conditions supposed, as, for example, after complete excision of the two thyroid lobes. On the contrary, the evidence from histology, as well as from embryology, seems to indicate that the two tissues are not only fundamentally different in structure, but possibly are also different in origin.

* Kohn : Archiv. für mik. Anatomie, Bd. 44, 1894.

On the physiological side Gley* was the first to prove the great importance of the parathyroids. He showed that in rabbits complete extirpation of the thyroid lobes alone is not followed by a fatal result so long as the parathyroids remain. Removal of both thyroids and parathyroids, however, is in most cases followed by typical symptoms of complete thyroidectomy ending in the death of the animal. This latter result has been contested by some observers, but renewed investigations have demonstrated its accuracy. Gley explained his results on the hypothesis that after removal of the thyroid its function is vicariously assumed by the parathyroids. He concluded, therefore, that the functional value of the two tissues is identical. Recent work, however, tends to throw doubt upon this conclusion. Vassale and Generali† state that in dogs and cats removal of all four parathyroids produces the acute symptoms of complete thyroidectomy, and finally causes the death of the animal, in spite of the fact that the thyroid body proper is left practically uninjured. On the other hand, complete removal of the thyroid lobes is not immediately injurious to the animal, provided the parathyroids—or in some cases, if even only one of the parathyroids —are left. They contend, therefore, that the result in dogs and cats usually attributed to extirpation of the thyroids is due in reality to the simultaneous removal of the parathyroids.

This result is partly confirmed by the independent experiments of Rouxeau‡ and of Gley.§ The former finds that in rabbits complete removal of the thyroids alone causes no trouble, at least no immediate trouble, while excision of the external parathyroids alone is followed frequently by death, or by convulsive symptoms. Gley reports some incomplete experiments upon rabbits and dogs that tend in the same direction. Finally, Moussu,‖ from experiments made upon mammals and birds, attempts to define in general terms the difference in function between thyroid and parathyroid tissue. According to his experiments, removal of the parathyroids alone is followed by certain acute troubles, such as have been usually described as the results of complete thyroidectomy, while removal of the thyroid lobes alone is followed by chronic troubles of nutrition which he designates as myxœdematous or atrophic

* Gley : Archives de Physiologie normale et pathologique, 1892.

† Vassale and Generali : Archives italiennes de Biologie, XXV. and XXVI., 1896.

‡ Rouxeau : Comptes rendus de la Soc. de Biologie, Jan. 9, 1897.

§ Gley : Ibid.

‖ Moussu : Ibid, Jan. 16, 1897.

cretinism. This last result has not been confirmed, so far as I am aware, by others, so that it cannot be accepted with entire confidence. It will be noted, however, that the tendency of this recent work is to show that the functional value of the thyroids and parathyroids is not identical, and that the importance hitherto attributed to the thyroids must be assigned, in part at least, to the parathyroids. The very great interest that these results may have when applied to human pathology and therapeutics will be evident to everyone.

Finally, a word may be said as to the possibility that other tissues exist in the body capable of replacing entirely or in part the functions normally performed by the thyroids or the parathyroids. This possibility seems to be indicated by the fact, commented on by most experimenters in this field, that occasionally animals are found in which apparently complete removal of all the thyroid tissue, including the parathyroids, is not followed by a fatal result. Such cases may be explained by assuming the existence of accessory thyroids or parathyroids that escape the attention of the operator, but it is also possible that they may be due to the fact that there are other organs in the body that possess a thyroid function. Experiments in this direction have been made upon the spleen and the hypophysis cerebri. With regard to the former organ the results may be considered as entirely negative, while as regards the hypophysis the evidence is unsatisfactory. Some details concerning this last organ will be presented later.

The results of recent physiological experiments upon the suprarenal bodies have not been less interesting, although less complete than those upon the thyroid. These curious bodies, like the thyroid, are found constantly in all classes of the vertebrates, and seem, therefore, to be organs of fundamental importance. As long ago as 1856 Brown-Séquard* stated that extirpation of both suprarenals is usually fatal to the animal, death occurring generally very shortly after the operation, more rapidly, according to this observer, than after removal of both kidneys. This statement has been questioned frequently by other observers, but the results of the renewed investigations that have followed upon the recent revival of interest in the physiology of the ductless glands seem to corroborate fully the account given by Brown-Séquard. In the case of dogs, according to Szymonowicz,† death follows the operation within fifteen hours.

* Brown-Séquard: Comptes rendus de l'Ac. des Sciences, XLIII., 1856. *Journal de la Physiologie*, I., 1858.

† Szymonowicz: Archiv. f. d. gesammte Physiologie, LXIV., 1896.

It has been shown, also, that in some species of animals accessory suprarenals are not uncommon, and it is possible that this fact may explain the survival of a certain number of animals after supposed complete extirpation of the suprarenals. Removal of only one suprarenal does not appear to cause any noticeable trouble. In the case of complete removal, followed by a fatal result, the prominent symptoms preceding death are extreme muscular weakness, asthenia, and, in the case of dogs examined during this period, a great fall in blood pressure, together with a feeble heart-beat. It will be noted that in cases of Addison's disease in man the important symptoms, in addition to the pigmentation, are also an asthenic condition of the muscles and the heart. What explanation have we to offer for the surprisingly profound effect produced upon the body by the removal of these small organs?

Unquestionably, the most significant facts with regard to this problem have been obtained from a study of the effects of injections of suprarenal extracts into living animals. A number of the earlier experiments of this kind, especially those performed upon rabbits, resulted in the death of the animal, the preceding symptoms being convulsive movements, followed by some paralysis. The really valuable results, however, have been obtained by a more exact study of the effects of such injections upon the vascular and respiratory organs. Most of our knowledge upon these points has been derived from the researches of Oliver and Schäfer,* and Cybulski and Szymonowicz.† These two sets of investigators published their results nearly simultaneously. The important facts determined by them, and since corroborated in many laboratories, are as follows: Extracts of the medulla of the suprarenal bodies injected into the veins of a living animal cause a pronounced slowing of the heart-beat and a large rise of blood pressure. If the animal is first given atropin to paralyze the inhibitory nerves to the heart, or if the vagi are previously cut, the injection causes usually a marked quickening, instead of a slowing of the heart-beat, and a greater, indeed often an extraordinary, rise of blood pressure. The respiratory organs are not affected so seriously, a temporary slowing and shallowing of the respiratory movements being the result usually noticed. The effect upon the heart and blood vessels is quite temporary. Its exact duration depends somewhat upon the dose,

* Oliver and Schäfer: *Journal of Physiology*, XVIII., 1895.

† Cybulski and Szymonowicz: *Gazeta Lekarska*, 1895. (Abstracted in Jahresb d. Thier-Chimie, 1895. Also Szymonowicz: Archiv. für d. gesammte Physiologie, LXIV., 1896.

and in part upon other less evident conditions, but, as a rule, within a very few minutes the rise in blood pressure, as well as the slowing of the heart-beat, passes off completely. New injections will bring out promptly a return of the effect described, although a continued repetition of the injections at too close intervals results in a progressive diminution of their action. Tying off the kidneys does not appear to prolong the effects of an injection, so that we may conclude that the temporary character of the result produced is not caused by a rapid elimination of the active substance through the kidneys, although, according to Szymonowicz, a part of it, at least, is got rid of by this means. The rapid disappearance, however, of the effects of a maximal or supramaximal dose indicates that the active substance is either quickly destroyed in the tissues or is neutralized in some other way.

The physiological explanation of the slowing of the heart caused by the suprarenal extracts offers no difficulties. Since this effect disappears completely upon section of the vagi, or after the injection of a few milligrams of atropin, it can only be due to a stimulating action upon the central endings of the inhibitory fibres, that is, upon the so-called cardio-inhibitory center in the medulla. According to Oliver and Shäfer the inhibitory effect is felt mainly upon the auricles. The beats of this part of the heart become weaker and slower and may cease altogether, while the ventricular beats, although slower, are more vigorous. After the vagi have been cut, suprarenal extracts cause a quicker, and according to Oliver and Schäfer, who measured the extent of the contractions directly, a stronger beat. This accelerating effect upon the heart after removal of the inhibitory fibres is not due, as we might at first suppose, to a stimulation of the central ends of the accelerator fibres, since it is still obtained after section of the cord in the neck, or after extirpation of the first thoracic ganglia. It must, therefore, be due to a peripheral action of the extracts upon the heart itself, either upon the muscle of the heart directly (Oliver and Schäfer) or upon the so-called motor ganglia (Szymonowicz, Gottlieb).

The effect of the injections upon the blood pressure has been explained differently by those engaged in the work. Both Oliver and Schäfer, and Cybulski and Szymonowicz, believe that the enormous rise in blood pressure is due mainly to a great constriction of the arterioles. According to the latter this constriction is brought about by a stimulating action of the extracts upon the vaso-motor centers in the medulla and cord, while according to Oliver and Schäfer the action is exerted directly on the muscles

of the blood vessels. Szymonowicz admits that if the cord is cut just below the medulla a great rise of pressure can still be obtained, but he explains this by supposing that the extract acts on the spinal centers. He asserts that if the entire cord is destroyed a rise of pressure can no longer be obtained. The experiment that he gives to illustrate this last point is, however, far from being convincing. The protocol of the experiment shows that the act of destroying the cord in itself reduced the blood pressure to zero. Moreover Biedl* reports that he has been able to get a rise in pressure from injection of the extracts after complete extirpation of the cord. The evidence, therefore, seems to favor the view proposed by Oliver and Schäfer, and this view is still further supported by the fact that when the volume of a limb is measured plethysmographically it often shows a distinct diminution after suprarenal injection, even though its nervous connections with the central nervous system are entirely severed.

There are, however, some facts reported in the experiments made by different observers which indicate that the assumed action of the substance on the peripheral arteries does not alone account for all the changes produced in blood pressure. It is probable that the greater force of the heart-beat plays an important part, as Gottlieb† contends, in causing the increase of arterial tension. Thus Szymonowicz reports measurements of the pressure in the external jugular vein made during one of his experiments. According to this report the venous pressure rose and fell with the arterial pressure, which is not what one would expect to occur in the case of a general constriction affecting the arterioles alone. According to Bayliss and Hill,‡ also, the general venous pressure increases with the rise in arterial pressure. So in a number of the published tracings given by Oliver and Schäfer it appears that the vasoconstriction was more pronounced in the abdominal viscera than in the limbs, since the volume of the latter measured plethysmographically showed an increase of a passive character, apparently, while the volume of the kidney or spleen was greatly diminished.

The significance of the marked reaction exhibited by suprarenal extracts depends very largely upon the possibility of proving that the substance producing the reaction is formed normally within the gland. It is conceivable, of course, that in the dead gland postmortem changes might cause the formation of a substance giving

* Biedl: Wien. klin. Wochenschrift, IX., 1896.

† Gottlieb: Archiv. f. exper. Pathologie u. Pharmakologie XXXVIII., 1897.

‡ Bayliss and Hill: *Journal of Physiology*, XVIII., p. 352, 1895.

this reaction, although under the normal conditions of life it might not exist. Fortunately, we have direct proof that the active substance in question is a normal product of the metabolism in the gland. Cybulski and Szymonowicz found that blood drawn from the suprarenal vein, when injected into the circulation of a normal animal, gives the same effect, although less in amount, as extracts of the suprarenal glands, while blood from other veins has no such action. This result has been denied by Oliver and Schäfer, apparently upon insufficient experimental grounds. Langlois,* on the contrary, has been able to corroborate this effect of suprarenal blood, and, in the laboratory at Baltimore, Dr. Dreyer has obtained clear proof of a similar action. It appears from Dreyer's experiments that the effect is not obtained in every animal, but in some cases the results are very positive, and in a matter of this kind the positive evidence is the most important. When we remember that we are dealing most probably with a material formed by the secretory activity of gland cells, and that the amount of this material may vary at different times or under different circumstances, it is not surprising that negative as well as positive results are obtained.

Since it seems certain that the substance does occur under normal conditions in the venous blood flowing from the glands, we are justified in concluding that it is a normal product of the metabolism of the medullary cells of the gland, and that it is discharged or secreted directly into the blood. It must, therefore, exert continually a stimulating effect upon the heart and blood vessels. In corroboration of this last conclusion we have some striking experiments recorded by Szymonowicz which show that after complete extirpation of the two glands the blood pressure becomes greatly depressed. Both Oliver and Schäfer, and Cybulski and Szymonowicz, conclude that the normal function of the suprarenals consists in furnishing this stimulating substance to the blood. The former observers believe that its effect is mainly upon the muscular tissue; that it has a general tonic or augmenting action on all varieties of muscle found in the body—the striated muscle as well as the cardiac and plain muscle tissue. Cybulski and Szymonowicz hold essentially the same general view, except that they believe that the substance acts upon the nerve centers controlling the muscular tissues rather than on these tissues directly. It is, perhaps, impossible at present to decide as to this detail. Oliver and Schäfer have shown, without much doubt, that the substance

* Langlois: Archives de Physiologie normale et pathologique, 152, 1897.

acts upon the blood vessels after their connections with the central nervous system have been completely severed, and, on the other hand, there is clear proof that it affects at least one part of the central nervous system, namely, the cardio-inhibitory center. Further experimenting will probably soon furnish more definite information upon the extent to which the muscular and the nervous tissues are affected by this substance. Upon either of the views proposed we can understand at once why removal of the suprarenals brings on a condition of muscular asthenia, and why the normal activity of these organs is so essential to the body as a whole. It is significant, in this connection, to recall that Oliver and Schäfer found that extracts of the suprarenals in cases of Addison's disease did not contain this stimulating substance. The hypothesis that the suprarenals secrete a stimulating substance that augments the tone of the muscular system, either directly or indirectly, is not the only one offered to explain the physiology of these bodies. According to some observers the main function of the suprarenals, like that of the thyroids, is to produce an antitoxic secretion capable of neutralizing or destroying certain poisonous products of body metabolism. The toxic products in this case have been supposed to originate in the functional metabolism of muscular tissue, and the asthenic condition following upon extirpation of the suprarenals has been compared with the similar effect produced by injecting the extracts of fatigued muscles into the circulation. The main argument of those who hold to this view seems to rest upon the fact that the blood of an animal that has been deprived of its suprarenals and is beginning to show the typical effects has a toxic effect when injected into the circulation of another animal from which the suprarenals have been removed shortly before. The fatal symptoms are brought on by the injection more rapidly than would happen otherwise. One cannot feel a great deal of confidence in this argument as contrasted with the apparently direct evidence offered in favor of the stimulation hypothesis.

Unfortunately, the physiological evidence with regard to the importance of the suprarenals to the body has not found so satisfactory an application in practical medicine as in the case of the thyroids. Suprarenal extracts and tissues have been used in cases of Addison's disease, but the beneficial effects obtained have not been so clear as in the case of thyroid extracts. Some of the results reported, however, indicate that the method is at least a hopeful one in certain cases.

A third interesting member of the group of ductless glands is

the hypophysis cerebri, and a few words may be said as to its supposed physiological activity. This gland is commonly described as consisting of two parts, the anterior and the posterior lobe. The histology and the embryology of the two parts indicate that they are entirely different in origin and in structure. The anterior lobe is evidently a glandular structure. It develops originally as a saccular invagination from the buccal epithelium and has essentially the same origin in all the vertebrates that have been examined. According to Haller* it is not strictly a ductless gland, since it possesses an imperfectly developed system of ducts that opens between the dura and the pia mater. It is evidently a secretory structure, and the fact that its secretion is discharged between the meningeal membranes suggests some special connection with the physiology of the brain. Histologically its structure recalls that of the thyroid gland, particularly in the fact that a colloidal material is said to occur frequently in the lumina of the gland tubules. In some animals, *e. g.*, the dog and the cat, it is a very small body, but in others, as the rabbit, sheep, ox and man, it is of considerable size and bears every indication in its structure of being an active secretory organ.

The posterior lobe, on the contrary, is very small in all animals and has the appearance of being a rudimentary organ. It develops as an outgrowth from the infundibulum of the brain and is more properly spoken of as the infundibular lobe or process. Its histology is very incompletely known. According to Berkley† it contains numerous typical nerve-cells, ependymal cells and neuroglia, a number of glandular epithelial cells arranged in part to form tubes or closed vesicles that contain a colloidal material, and some curious structures resembling nerve end-organs.

The observations bearing upon the functions of the hypophysis have been limited to the glandular lobe. On the pathological side it has been shown that in many, if not in most, of the cases of acromegalia the glandular lobe exhibits pathological changes. For this reason extracts of the gland have been used therapeutically in cases of acromegalia, and, according to some reports, benefits have followed the treatment to the extent that some of the disagreeable features have shown amelioration. The evidence from this side, however, is not satisfactory, and the nature of the connection between acromegalia and disturbance of the function of the hypophysis, if any exists, needs more complete investigation.

The experiments made by the physiologists are also meagre and

* Morphologisches Jahrbuch, XXV, 1896.

† Berkley: The Johns Hopkins Hospital Reports, IV., 1895.

inconclusive. Gley* reports a set of experiments made upon rabbits, in which he attempted to destroy the gland by an operation from above. The experiments were made upon rabbits from which the thyroid lobes had been removed previously, with the idea of demonstrating that a similarity in function exists between the thyroid and hypophysis. All but one of the animals died, owing to the severity of the operation. In the single survivor it was noted that the animal exhibited at times spasmodic muscular contractions and some degree of paresis, and that it died about a year after the operation. On the assumpton that the animal would have lived if the thyroid lobes alone had been removed, Gley concluded that the removal of the hypophysis had prevented the parathyroids from replacing completely the loss of the thyroid, and that, therefore, the hypophysis is related in function to the thyroid tissue. Naturally but little importance can be attached to a single experiment of this kind, and, so far as I know, the author has not repeated the investigation. Vassale and Sacchi† claim to have removed the hypophysis partially or completely in a number of animals by an operation through the base of the skull. In cases of complete removal the animal died within a short time—fourteen days or less—after exhibiting a number of symptoms similar to those caused by thyroidectomy, such as muscular tremors and spasms and the development of a cachectic condition. Most physiologists, I fancy, will accept these experiments also with some hesitation until they have been confirmed by other observers. The very severe character of the operation necessary to reach the gland makes it questionable whether the results reported were due to its removal alone, although the experiments were evidently made with great care.

Szymonowicz and also Oliver and Schäfer report experiments upon the effects of injections of extracts of hypophysis into the circulation of normal animals. Szymonowicz states that in two experiments he obtained a slight fall pressure and a quickening of the heart-beat. He concludes, therefore, that the physiological action of these extracts is opposed to that caused by extracts of the suprarenals. Oliver and Schäfer, on the contrary, report that extracts of hypophysis exert an effect very similar in some ways to that shown by suprarenal extracts. For instance, they cause a marked rise of blood pressure, together with an augmentation of the heart-beat. Unlike the suprarenal extracts, however, they do not produce a slowing of the heart-rate when the vagi are intact.

* Gley: Archives des Physiologie normale et pathologique, 1892. 311.

† Vassale and Sacchi: Archives ital. de Biologie, XXII., CXXXIII., 1895; also XVIII., 1893.

Upon the basis of these incomplete experiments they draw the somewhat hasty conclusion that the hypophysis and the thyroid are not similar in function, and that the hypophysis is not capable of assuming vicariously the activities of the thyroid.

I have recently made a number of experiments upon this organ, the results of which have been quite uniform and in many respects very different from those obtained by the authors just quoted. My experiments were made with the hypophysis of the sheep mainly, although at first the gland of the dog was also used. The extracts were made in normal saline, or in glycerine followed by dilution with normal saline, and usually the fresh gland was employed. The experiments differed from those reported by others, in that extracts were made separately of the glandular and the infundibular lobe, and the physiological effects of each were tested by injection into the circulation of normal dogs. It was found that the extracts of the glandular lobe have little or no perceptible effect when injected alone. Extracts of the small infundibular lobe, on the contrary, have a distinct and remarkable effect upon the heart-rate and blood pressure, an effect which resembles in some respects and differs in others from that shown by suprarenal extracts.

Briefly stated, these extracts injected into the normal animal with its vagi intact cause a very pronounced slowing of the heart-beat, similar to that caused by suprarenal extracts, but lasting a much longer time. The heart-beat is not only slowed, but is considerably augmented in force, as is shown by tracings taken with a Hürthle manometer. At the same time the blood pressure rises to a considerable extent, owing, apparently, to a peripheral constriction of the blood vessels, since oncometric tracings from the kidney show that this organ shrinks greatly in volume. Usually the constriction of the blood vessels occurs first, so that the pressure rises for about 20 mms. or more of mercury. This is succeeded sometimes by a temporary fall of pressure during which the heart-rate may be increased, and then the slowing of the heart begins, while the pressure rises again to a greater or less extent above the normal. This last effect continues for a relatively long time and passes off gradually. The slowing of the heart may continue for half an hour or longer. If the dose used is a maximal one, and a second injection is given too quickly afterward, little or no effect is obtained. If, however, the dose is not too strong, and sufficient time is given for its action to wear off, a repetition of the effect is obtained, and this may occur a number of times, although the effects decrease progressively in intensity.

The effects of the injection are somewhat different if the vagi are previously cut, or if a little atropin is given to paralyze the inhibitory fibres. Under these circumstances the slowing of the heart-rate is very much less marked, although not entirely lacking. In round numbers it may be said that with the vagi intact the heart-rate is reduced about 50 per cent., while in the atropinized animal the reduction is about 20 per cent. It might be added that an animal deeply under ether alone behaves in this respect like an animal with its vagi cut. This result indicates that the slowing of the heart-rate in the normal animal is due in part, but only in part, to a direct action on the medullary centers of the inhibitory fibres. On the other hand, the rise of blood pressure after section of the vagi is greater. Usually the blood pressure rises rapidly for about 20 mms. of mercury; this is succeeded in some cases by a temporary fall, and then the pressure again rises rapidly, reaching a height, in some cases, nearly equal to that caused by suprarenal extracts. During this last phase the heart-beats are slower and more powerful, the effect in this respect differing from that caused by suprarenal extracts. The effect lasts longer than with suprarenal extracts, and a longer interval must be allowed before a new injection will give the same result. I have obtained a marked rise of pressure from injection of extracts of the infundibular lobe, after severance of the cord below the medulla, and in one case after removal of most of the thoracic part of the spinal cord in addition, thus indicating that the constriction of the blood vessels is probably a peripheral effect, and not due to stimulation of the vaso-motor centers. These observations that I present here only incompletely may be taken to indicate that the infundibular lobe of the hypophysis is, in all probability, not a rudimentary organ, but a structure that has some important physiological activity. Moreover, its function is probably different from that of the glandular lobe, and possibly quite independent of it. With regard to the function of the grandular lobe, the method of injecting extracts into the circulation of a normal animal seems to teach us nothing. While the negative results thus obtained do not oppose, they cannot be said to support, the favorite hypothesis that this part of the hypophysis cerebri has a function resembling that of the thyroid lobes. I venture to suggest that this supposed similarity in function might be tested most satisfactorily upon human beings by feeding the gland in cases of myxœdema or goître and ascertaining whether a reaction similar to that caused by the thyroid can be obtained.

INTERNAL SECRETIONS CONSIDERED IN THEIR PHYSIOLOGICAL, PATHOLOGICAL AND CLINICAL ASPECTS.

Considered from a Chemico-Physiological Standpoint.

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In considering this subject from a chemico-physiological standpoint allow me at the outset to emphasize the fact, now well established, that the symptoms which follow the simple removal of a physiologically active gland from the body result wholly from the loss of the gland. You may recall that when attention was first drawn to the possibility of producing the typical symptoms of myxœdema in monkeys by removal of the thyroid gland, there was a tendency to assume injury to the sympathetic or other nerves of the neck as an explanation of the phenomena, rather than to admit the possibility even of a general or limited disturbance of the metabolism of the body through chemical changes associated with removal of the gland. It was not until the experiments of Murray made clear the fact that the effects resulting from the removal of the thyroid in man could be overcome, in part at least, by administration of the gland-substance, that scientific investigation took the proper turn and a full realization of the possible importance of the so-called ductless glands and their internal secretions began to dawn upon the mind. To-day, however, we recognize their functional activity as a necessary element for the welfare of the body. Their removal, or any impairment of their function, may produce even more disturbance of physiological equilibrium than a corresponding disarrangement of glands formerly considered of greater physiological value. Further, it needs to-day little argument to support the view that such power as these physiologically active glands possess is due to definite chemical compounds elaborated by the glands as products of their individual secretory or metabolic activity. As with other glands having more obvious functions, the secreting cells plainly manufacture certain specific products, but in the case of the internal secretions these products find their way into the blood and lymph, by which they are distributed throughout the body, and thus made available either in con-

trolling or regulating the general nutrition of the economy or to serve some more specific purpose of equal importance for the welfare of the organism. This being so, it is equally probable that in the general and specific metabolism going on in all the tissues and organs of the body the various products formed and absorbed by the blood and lymph may contribute somewhat to the welfare of the body prior to their excretion. In its broadest sense, therefore, internal secretion must be looked upon as something common to all active tissues, the ordinary katabolic products of both circulating and morphotic proteids, for example, no doubt exerting some physiological action during their transit from the place of their formation to the organ which serves for their excretion. It is well, perhaps, to give full recognition to this possibility, for physiological equilibrium in the broadest sense is clearly dependent upon the harmonious action of a large number of related parts, and experiment only can determine, and perhaps then imperfectly, how far the products of one gland or tissue are essential for the well-being of the whole. We know, however, that certain organs with the products they elaborate can be dispensed with, while the removal of other organs involving no greater surgical interference is quickly followed by marked disturbances and later by death. Czerny had no difficulty in removing the stomach from dogs, the health of the animals remaining unimpaired when the œsophagus was properly joined to the intestine. Similarly, Schäfer and Moore* have recently shown that both parotids and both submaxillary glands may be removed from the dog without any disturbance of nitrogenous metabolism, or without any apparent effect upon carbohydrate digestion. Evidently these glands do not possess any intrinsic internal secretion necessary to the life of the animal or having any important action on the metabolic processes of the body. If they do furnish an internal secretion it obviously must be one common in function to that supplied by some other organ. In the present discussion, therefore, we may advantageously limit the term "internal secretion" simply to those specific products which, being manufactured in certain definite glands, are plainly endowed with well-defined physiological action.

Let us first consider the thyroid gland, upon which more work has been done than upon any other similar structure. Dating from 1883, when Kocher and Reverdin published their well-known observations on the effects of thyroidectomy in the human subject, it has gradually become apparent that there are two distinct ways

* Proceed. Physiol. Soc.; Journal of Physiol., Vol. 19, No. 4.

in which the effects of the operation may be manifested.* Thus, in some animals, as in most carnivora, complete removal of the thyroidal tissue is followed by a rapid development of symptoms indicating a marked irritation of the nervous and muscular systems as manifested by tetanus, epileptiform convulsions, etc., terminating in death. In other cases slowly developing changes are observed corresponding to myxœdema. Hence, in some animals thyroidectomy is followed by such a marked disturbance of physiological balance that death results very quickly, while in others the development of symptoms is very slow, giving rise to chronic effects which may endure for months. Evidently, aside from the more acute and toxic effects which may immediately follow the operation, there are more gradual disturbances of metabolism which eventually lead to the complete breaking down of the animal. That the symptoms thus produced are dependent upon the withdrawal from the system of certain specific products is evident from the fact that after extirpation of the thyroidal tissue the mere feeding of thyroid glands, or the subcutaneous and intravenous injection of thyroid extracts, suffices to quickly dispel the myxœdemal swellings, the rough thickened condition of the skin, the muscular and mental apathy, etc.† With dogs the convulsions which follow extirpation of the thyroids are quickly checked by the subcutaneous injection of thyroid extracts. Experiments along these lines with extracts of dead tissue have, as you know, made it very evident that the thyroid gland forms some one or more specific substances, the absence of which from the body sooner or later renders life impossible. Where, however, the animal, as a dog, is provided with accessory thyroids the entire thyroid gland may be removed without death resulting, providing one of the parathyroids is left, but if both parathyroids are excised then 40 per cent. of the thyroidal tissue proper must be left in order to have the dog live.‡ Evidently, the thyroids and accessory thyroids have more or less of a common function, the one being able to fulfil the purpose of the other to a certain degree; a fact which in itself may be taken as evidence of the

*Compare Roos: Ueber die Einwirkung der Schilddrüse auf den Stoffwechsel nebst Vorversuchen über die Art der wirksamen Substanz in derselben. Zeitschr. f. physiol. Chem., Band 21, p. 19. This paper contains numerous references.

†See Kent: Thyroid extract after Thyroidectomy. Proceed. Physiol. Soc.; Journal of Physiol. Vol. 15. Also Meltzer: Ueber Myxödem. Centralbl. f. Physiol., 1894, p. 698.

‡Edmunds: Observations on the Thyroid and Parathyroid of the Dog. Journal of Physiol., Vol. 22. Proceed. Physiol. Soc., June 27, 1896.

importance of thyroidal tissue and the care exercised by nature in preventing its complete suppression.

The very nature of the physiological results which follow the removal or accompany the atrophy of the thyroidal tissue suggests the formation of one or more toxic substances to which the well marked symptoms are due; substances which are either not formed in the presence of thyroidal tissue or else being formed are either neutralized (physiologically) or decomposed and rendered inert by substances furnished by the thyroid gland. Such a view obviously implies a difference in the character and possibly in the extent of the metabolic changes going on in the body, and we may, therefore, advantageously consider the character of our knowledge upon this subject. A careful study of the literature shows quite clearly that certain definite statements are justified. Thus, Leichtenstern and Wendelstadt* found by feeding thyroid glands to healthy obese individuals that a marked loss of body-weight resulted. Roos,† experimenting with normal dogs, observed that in feeding the gland substance for several days there was a marked increase in the excretion of nitrogen through the urine, also of sodium chloride and of phosphoric acid (P_2O_5). On dogs with the thyroids removed, this action was still more marked, so far as the excretion of nitrogen and chlorine was concerned, also in the loss of body-weight and in the excretion of water, but the excretion of phosphorus fell behind the normal. Further, in an experiment with a goitre-patient, otherwise healthy, Roos observed on feeding thyroid glands a similar tendency towards increased excretion of nitrogen and chlorine with a marked increase in the output of phosphoric acid. Mendel, Napier, Ord and others, making observations on myxœdema patients, likewise noted that the use of thyroid preparations by subcutaneous injection, by glycerin extracts, etc., as a rule, not only led to a betterment of the symptoms, but gave rise to a marked diuresis, loss of body-weight and increased excretion of nitrogen or urea. Denning,‡ likewise, found that while different individuals reacted somewhat differently under thyroid feeding, yet there was a general tendency toward increased excretion of nitrogen as well as a loss of body-weight. It was also noted that the excretion of nitrogen and urea was not always parallel. Occasion-

*Ueber Myxœdem und Entfettungskuren mit Schilddrüsenfütterung. Deutsch. med. Wochenschr., 1894, No. 50.

† Loc. cit.

‡ Ueber das Verhalten des Stoffwechsels bei der Schilddrüsentherapie. Münchener med. Wochenschr., 1895, No. 17. Also No. 20.

ally albumin and sugar appeared in the urine. In one case the volume of urine excreted rose at once 200 cc. per day, the pulse rate increased 22 per cent., while the nitrogen excreted rose 15 per cent. during the feeding period. Similarly, in Basedow's disease, Scholz* observed under the influence of thyroid feeding in a patient 29 years old, diuresis, increased excretion of nitrogen and sodium chloride with a marked decrease in the excretion of phosphoric acid. Magnus Levy† likewise records that a healthy individual taking thyroid tablets for 19 days lost 7 pounds body-weight with some increase in O_2 and Co_2 exchange. In three cases of Basedow's disease, on the other hand, oxygen consumed and carbonic acid excreted were greatly in excess of the normal. Fritz Voit,‡ by carefully conducted experiments on healthy dogs, found that the feeding of fresh thyroid glands produced a marked increase in the output of carbonic acid as well as of nitrogen. Michaelson§ found after extirpation of the thyroid in hungry cats the Co_2 excretion increased, while J. L. Smith‖ has observed that when thyroidectomy is performed on cats there is a marked disturbance of the heat-regulating mechanism.

From these and other observations that cannot be recorded here it is very plain that the administration of thyroid gland and thyroid extracts to normal individuals, and especially to thyroidectomized animals and individuals in whom the thyroid glands are diseased, produces a very noticeable effect upon the metabolism of the body, leading to a marked loss of body-weight, an increased excretion of water, nitrogen and carbonic acid, and also of sodium chloride. This great diminution of body-weight is by no means due wholly to loss of water nor to removal of fat, for if a healthy individual is fed upon a diet rich in fats and carbohydrates the well-known proteid-sparing power of the latter foods is not able to keep down

* Ueber den Einfluss der Schilddrüsenbehandlung auf den Stoffwechsel des Menschen insbesondere bei Morbus Basedowii. Centralbl. f. innere Med., Band 16, p. 1041 and p. 1069.

† Ueber den respiratorischen Gaswechsel unter dem Einfluss der Thyreoidea, sowie unter verschiedenen pathologischen Zuständen. Berliner klin. Wochenschr. 1895, p. 650. See also Richter: Zur Frage des Eiweisszerfalles nach Schildderüsenfütterung. Centralbl. f. Physiol., Band 10, p. 49. Also Ducceschi: Beitrag zur Erforschung der Stoffwechselvorgänge bei thyroidectomirten Thieren. Ibid., Band 10, p. 217.

‡ Stoffwechseluntersuchungen am Hund mit frischer Schilddrüse und Jodothyrin. Zeitschr. f. Biol., Band 35, p. 116.

§ Jahresbericht f. Thierchemie., Band 19, 335.

‖ On some effects of Thyroidectomy in animals. Journal of Physiol., Vol. 16, p. 378.

the loss of nitrogen when thyroids are administered. Proteid material is still broken down in increased quantity, and not from any individuality of the person experimented upon, but plainly under the exciting influence of the thyroid.* The gland substance evidently causes an increased decomposition of the tissue proteids, thus showing a certain resemblance to the action of phosphorus on the organism (Roos). At the same time the loss of body-weight under thyroid feeding is far greater than can be accounted for by the increased proteid decomposition, from which, in conjunction with the increased gaseous exchange, we must infer an increased breaking down of fatty tissue in accord with the prevalent idea that thyroids tend to reduce obesity. This, furthermore, is in harmony with the well-known fact that increase in proteid metabolism is almost invariably associated with increase in the metabolism of non-nitrogenous matter.

The significance to be attached to this increase in proteid metabolism, however, is, I think, something more than a mere quantitative one. The very fact that there are quantitative changes renders it quite probable that there are also qualitative changes, and that the presence or absence of the thyroid gland or its equivalent from the body may modify the *line* of metabolism. Upon this point, however, we know very little; we simply infer. Still there are some facts in connection with the proteids of the blood which are worthy of a moment's consideration. Thus, it has been shown by comparison of the proteids of a normal dog's blood with those present in the blood after extirpation of the thyroids, that in the period preceding the convulsions the percentage amount of serum-albumin is increased and the globulins decreased. In the second period, on the other hand, when the cramps or convulsions appear up to the end, there is a progressive increase in the amount of globulin and a decrease of serum-albumin as well as of the total proteid. Hence, there is at first an increase and then a decrease of the albumin quotient. From this it would appear that in the first stages there is an abatement of the metabolism of the tissues, followed by an increase, and that possibly in the incomplete breaking-down of the proteid material intermediate toxic products appear which are the cause of the cachexia.† Further, according to

* Bleibtreu und Wendelstadt. Stoffwechselversuch bei Schilddrüsenfütterung. Deutsche med. Wochenschr., 1895, p. 348.

† Beitrag zur Lehre über die Function der Schilddrüse, Jahresbericht f. Thierchemie, 1895, p. 375.

Formánek and Haskovec,* in the thyreopriva cachexia, resulting from the extirpation of the thyroids in dogs, the number of red blood corpuscles is systematically diminished, while the leucocytes are increased, and the dry residue of the blood as well as the iron and hæmoglobin are diminished. In connection with the diminution of hæmoglobin there is an acceleration of respiration and of the pulse, which, however, in the terminal stages of the cachexia diminishes. The iron liberated by the decomposition of the red blood corpuscles is deposited in the organs of the body, especially in the spleen and lymph glands. If the blood is taken for examination during a convulsive seizure, on the other hand, it shows a reversal of the above conditions; it is thicker, contains more solid matter, as well as iron and hæmoglobin. If extract of the thyroid is injected into the operated animal there is an immediate increase in the number of red corpuscles and a betterment of the animal's condition. Hence, the thyroid is evidently concerned in hæmatosis, and it is quite possible that the decomposition of the blood which takes place induces certain alterations in the formation of the end-products of metabolism, so that poisons result which give rise to intoxication of the organism. Just here it may be mentioned that some recent observations on the feeding of thyroids in insanity tend to show that the percentage of the small mononuclear cells or lymphocytes of the blood are increased while the multinuclear neutrophiles are correspondingly diminished under the action of the drug, thus suggesting that the gland-tissue or its active principle has a direct stimulating influence upon those tissues of the body directly concerned in the production of the lymphocytes, viz., the lymphatic or adenoid tissues.†

In addition to these changes, emphasis must be laid upon the apparent connection between the thyroid gland and phosphoric acid metabolism. Thus, the increased excretion of P_2O_5 after feeding thyroids to normal animals, and the great decrease in the case of animals with the thyroids removed, is naturally suggestive. The facts may be explained in two ways: either the metabolism of phosphoric acid and its excretion are retarded in the absence of the gland, so that there is a retention of P_2O_5 in the body, or else the organism can assimilate sufficient phosphoric acid only in the presence of the substance or substances furnished by the thyroid

* Ducceschi: Ueber die Bluteiweisstoffe des Hundes im Verhältniss mit den Folgen der Schilddrüsenextirpation. Centralbl. f. Physiol., Band 9, p. 359.

† Perry: Some studies of the blood in Thyroid feeding in Insanity. *Medical Record*, August, 1896.

gland (Roos). It has been suggested, as you know, that the activity of the thyroid gland is a toxic one, but that this action is normally paralyzed by some one or more products of its own metabolism. The view that in the absence of the thyroid gland not enough P_2O_5 can be assimilated for the wants of the body finds a certain degree of confirmation in some of the symptoms noticeable in cretinism and myxœdema; viz., the retardation in bone-development and the slow calcification in cretinism. On the other hand, the tendency towards tetanus might perhaps be explained on the ground of an acute P_2O_5 retention in the central nervous system similar to that of uræmia; or, equally plausible, as due to a marked deficiency of P_2O_5 in this tissue. Thus, in Basedow's disease the observations of Kocher, that administration of sodium phosphate leads to a marked betterment of all the symptoms, are directly pertinent.

Further, we must not overlook the fact clearly shown by Halliburton,* in connection with Horsley, that after thyroidectomy there is a distinct tendency toward an increase in the percentage of mucus in the tissues of the body, especially marked in the connective tissues and salivary glands. While this increase is not as great as at one time thought, it is still distinctly recognizable and affords additional evidence that the thyroid plays some important part in the katabolic processes of the body, and that when it is removed or diseased the normal chain or rhythm of metabolism is broken. As to the chemical nature of the products which are directly responsible for the results attending thyroidectomy or associated with a morbid condition of the thyroid we have no direct knowledge, and as to their physiological character we can only infer from the nature of the symptoms which result. It is to be presumed that the toxic products are formed not in the thyroid, but in the tissues of the body and as a result of preverted metabolism due to atrophy or alterations of the thyroid gland. The latter evidently furnishes something which either directly neutralizes toxic products common to the body, or far more probably prevents their formation through an influence upon the line of metabolism, or to give due weight to all the views which have been advanced, both suggestions may be correct.

What now is the chemical and physiological character of the protective products which thyroidal tissue evidently manufactures? To this question there are many conflicting answers; still out of the

* See Halliburton's Handbook of Chemical Physiol., p. 505.

chaotic mass of material available I think it is possible to draw certain definite conclusions. In the first place it must be remembered that the epithelial cells of the thyroid gland apparently manufacture a so-called colloid secretion which evidently finds its way into the blood through the lymph, presumably carrying with it the active principles. This secretion obviously cannot be collected for study, but such active principles as it contains may be sought for in the gland itself, since we have every reason to believe in their ready solubility. By histological methods applied to sections of the thyroid it has been shown that the colloid matter gives the general proteid reactions, that it is very soluble in dilute alkaline fluids and readily dissolved by gastric digestion.* Our knowledge of the chemical composition of the thyroid gland, and hence presumably of the colloid secretion, is due mainly to the work of Bubnow,† Gourlay,‡ Notkin,§ Moscatelli,‖ Fränkel,¶ and especially Baumann and Roos,** and Hutchinson.†† To briefly summarize the present state of our knowledge, ignoring minor points of difference, I think it is quite clear that the thyroid gland is especially characterized by the presence of a compound proteid of peculiar constitution, and that this substance which Hutchinson calls 'colloid matter' is the active constituent of the gland. There is also present another proteid, a nucleo-albumin, in small amount, which Hutchinson considers as probably contained in the cells of the acini. In addition there are certain extractives to be found, viz., xanthin, hypoxanthin, inosite,‡‡ volatile fatty acids, paralactic acid, succinic acid and calcium oxalate; bodies, however, of no special physiological significance.

* Langendorff: Beitrag zur Kenntniss der Schilddrüse. Du Bois-Reymonds Archiv. f. Physiol., 1889, Supplementheft, p. 219.

† Beitrag zur d. Untersuchung der chemischen Bestandtheile der Schilddrüse des Menschen und des Rindes. Zeitschr. f. physiol. Chem., Band 8, p. 1.

‡ The Proteids of the Thyroid and the Spleen. Journal of Physiol., Vol. 16, p. 23.

§ Zur Schilddrüsen-Physiologie. Virchows Archiv., Band 114. Supplementheft, p. 224.

‖ Beiträge zur Kenntniss der Milchsäure in der Thymus und Thyreoidea. Zeitschr. f. physiol. chem., Band 12, p. 416.

¶ Thyreoantitoxin, der physiologisch wirksame Bestandtheile der Thyreoidea. Wiener klin. Wochenschr., 1895, No. 48.

** Ueber das normale Vorkommen des Jods im Thierköper. Zeitschr. f. physiol. Chem., Band 21, p. 319 and 481. Band 22, p. 1.

†† The Chemistry of the Thyroid Gland and the nature of its active constituent. Journal of Physiol., Vol. 20, p. 474.

‡‡ Tambach: Pharmaceutische Centralhalle, March, 1896.

The chief interest centers around the above mentioned proteid material, which is plainly of a peculiar kind, since it tends to hold a certain amount of iodine in combination and yields on decomposition a peculiar non-proteid substance carrying with it most, if not all, of the iodine and endowed with marked physiological action. This latter substance, to which Baumann has given the name of thyroiodin, later changed to iodothyrin, is especially characterized, chemically, by its great resistance to ordinary decomposing agents. Digestion of the thyroid gland with active gastric juice yields the iodothyrin as an insoluble residue, but still active. The gland can even be boiled an entire day with ten per cent. sulphuric acid without loss of the active principle, the latter separating from the cooled fluid as a fine flocculent precipitate almost wholly insoluble in cold water and acid, soluble in hot alcohol and readily soluble in dilute alkalies. When purified by repeated precipitation, re-solution, etc., the body may contain as much as ten per cent. of iodine. In the gland, according to Baumann, iodothyrin exists in great part combined with albumin and in smaller amount with globulin, and these compounds are likewise physiologically active, although less so than the iodothyrin itself. The iodothyrin of Baumann is thus a non-proteid cleavage product of a more complex body, naturally present in the gland and characterized by containing both iodine and phosphorus (0.5 per cent.). Aqueous and glycerin extracts of the gland contain iodothyrin or the mother-substance, although they do not take up all of the substance. Extraction of the gland with 0.75 per cent. sodium chloride solution, frequently repeated, removes all of the iodine-containing substance, and the residual tissue has little or no effect upon goitre.*

That iodothyrin possesses all the peculiarities associated with thyroid-therapy is, I think, pretty thoroughly established. The experiments of Roos† upon animals, and the clinical observations of Leichtenstern and Ewald have clearly demonstrated the physiological power of the substance. Its action on goitre,‡ as tested in over a hundred cases, is very noticeable. In the parenchymatous form a few days' treatment suffices to greatly reduce the size of the swelling. Normal dogs in nitrogenous equilibrium,

* Roos: Zur Frage nach der Anzahl der Wirksamen Substanzen in der Schilddrüse. Münchener med. Wochenschr., 1896, p. 1157.

† Ueber die Wirkung des Thyrojodins. Zeitschr. f. physiol. Chem., Band 22, p. 18.

‡ See Ewald und Bruns: Verhandlungen des Congresses für innere Medicin, 1896, p. 101.

treated with iodothyrin, suffer a marked loss of body-weight, an increased excretion of nitrogen, NaCl and P_2O_5, while diuresis is equally marked (Roos). Further, comparative experiments by Fritz Voit,* most carefully conducted on dogs in nitrogenous equilibrium, with fresh thyroid and iodothyrin show that the latter has practically the same action as the former in increasing the decomposition of fat and in stimulating the metabolism of proteid matter. In myxœdema the physiological action of iodothyrin is equally pronounced. Thus, in one case,† a 16-year-old patient received for 6 days 2 grams of iodothyrin (=0.6 milligram iodine) daily. In the fore-period of 3 days she received 18.02 grams of nitrogen and excreted 17.88 grams. In the iodothyrin period she ingested 16.2 grams of nitrogen and excreted 20.0 grams, while in the 3 days after-period she consumed 15.65 grams of nitrogen and ingested 21.59 grams. In 10 days the body-weight fell 4 pounds. In the treatment of obesity iodothyrin has likewise been effective.‡ It has also been clearly established by experiments on dogs that iodothyrin will cut short the various symptoms produced by thyroidectomy, noticeably the convulsions.§ As Baumann and Goldmann‖ have shown, dogs with thyroids removed do not manifest symptoms of tetanic convulsions so long as iodothyrin is given regularly each day in doses ranging from 2 to 6 grams. Further, in such cases the withdrawal of the iodothyrin, or a marked reduction in the amount administered, is generally followed by an appearance of the convulsions. The dosage required to remove or overcome the tetanus of a dog suffering from thyroidectomy is greater the more vigorous the symptoms and the longer the administration has been delayed after the appearance of symptoms. The negative results obtained by Gottlieb¶ have been recently shown to be due to the employment of a poor preparation.

* Stoffwechseluntersuchungen am Hund mit frischer Schilddrüse und Jodothyrin. Zeitschr. f. Biol., Band 35, p. 116.

† Treupel: Stoffwechseluntersuchung bei einem mit Jodothyrin (Thyrojodin) behandelten Falle von Myxoedem und Mittheilung einiger Thierversuche mit Jodothyrin (Thyrojodin). Münchener med. Wochenschr., XLIII. 38, p. 885. See also Notkin, Virchow's Archiv., Band 144, Supplementheft.

‡ See Grawitz: Beitrag zur Wirkung des Thyrojodin auf den Stoffwechsel bei Fettsucht. Münchener med. Wochenschr., 1896, No. 14. Also Henning Ibid., 1896, No. 19.

§ Hoffmeister: Deutsch. med. Wochenschr., 1896, No. 22. Hildebrandt: Berliner klin. Wochenschr., 1896, No. 37.

‖ Ist das Jodothyrin (Thyrojodin) der lebenswichtige Bestandtheil der Schilddrüse? Münchener med. Wochensch., 1896, p. 1153.

¶ Deutsch. med. Wochenschr., 1896, No. 15.

Does the physiological action of the thyroid gland reside wholly in this so-called iodothyrin or its antecedent? In attempting to answer this question we must give a moment's attention to Fränkel's so-called thyreoantitoxin.* This, as you may remember, is a crystalline body of neutral reaction obtained from the proteid-free extracts of the thyroid gland. It is soluble in water and alcohol, but precipitable by ether and acetone, and from its composition it has been suggested that it is a guanidin derivative. Fränkel ascribed to this substance the physiological activity of the thyroid gland, since he obtained a suspension of convulsions with thryoid-ectomized cats on injecting this body. Further, Drechsel† has made a preliminary communication to the effect that the proteid-free extract of the thyroid from pigs contains two crystalline substances in small amount, which when fed to thyroidectomized animals appear somewhat active, although not strongly so. Drechsel therefore suggests that possibly there may be three active substances present in the thyroid, viz., two bases, one identical with Fränkel's antitoxin, and Baumann's iodothyrin. He would thus ascribe to the thyroid several associated functions and corresponding to each a distinct chemical substance. Theoretically, of course, this is quite plausible, but Drechsel's compounds have not been further heard from and there are many recent observers who fail to find any physiological action whatever with the proteid-free extract from the gland.‡ Moreover, careful comparative study of the action of thyreoantitoxin and iodothyrin in a myxœdema patient showed that while the former was entirely without beneficial action the latter produced all the results characteristic of thyroid feeding.§ Further, Roos,‖ by experiment on a normal dog in nitrogenous equilibrium, found that thyreoantitoxin was wholly without influence on metabolism, while iodothyrin given to the same animal under like conditions caused at once a marked increase in the output of nitrogen, NaCl and P_2O_5. In other words, thyreoantitoxin shows with certainty none of the properties of the thyroid gland, while iodothyrin is apparently the physiological equivalent of the gland. Indeed, in its action on goitre iodothyrin is more effective than the

* Wiener klin. Wochenschr., 1895, No. 48.

† Die Wirksame Substanz der Schilddrüse, Vorläufige Notiz. Centralbl. f. Physiol., Band 9, p. 705.

‡ See Hutchinson: The chemistry of the Thyroid Gland and the nature of its active constituent. Journal of Physiol., Vol. 20, p. 491.

§ Magnus Levy: Deutsche med. Wochenschr., 1896, No. 31.

‖ Münchener med. Wochenschr. 1896, No. 47.

gland itself, since when the gland is taken it must first undergo digestion to liberate the iodothyrin and some may be lost by putrefactive changes in the intestine.

What now is the significance of the iodine contained in the so-called iodothyrin? Iodine is not a common constituent of the animal body, and its discovery by Baumann in the thyroid gland toward the end of 1895 was the first intimation of its presence in the human organism. So far as known, it is not normally present to any extent in other tissues.* Traces, however, are found in the thymus of the calf (Baumann).† Barrell has likewise reported the presence of traces in the spleen, adrenals and the ovaries of pigs and cows. The amount, however, is very small as compared with that found in the thyroid. Calling the amount of iodine in 1 gram of fresh thyroid as 1, the spleen contains $\frac{1}{20}$, the adrenals $\frac{1}{130}$, and the ovaries $\frac{1}{62}-\frac{1}{65}$ per gram of fresh tissue. Iodine has likewise been detected in the human hypophesis.‡

In human thyroids, on the other hand, as well as in the thyroids of sheep, oxen and pigs, iodine is most generally present in quite appreciable amount, and pure iodothyrin may contain as much as 10 per cent. of the element. In iodothyrin the iodine is in close combination with the rest of the molecule and is not easily split off even by the action of alkalies. It is noticeable that the thyroids of sheep (and of other animals) vary greatly in their content of iodine. Thus in sheep coming from Freiburg 1 gram of dry thyroid gland contained on an average 0.9-1.3 milligrams of iodine, while the thyroids from Paris sheep contained 1.15-1.2 milligrams of iodine per gram of dry gland, and those from Elberfeld 1.5-5. milligrams per gram of dry tissue. As judged by the rate and intensity of physiological action 0.25-0.3 milligram of iodine in the form of iodothyrin is equal to 1 gram of fresh thyroid gland. Further, according to Baumann, doses of 1 milligram of iodothyrin which contain only $\frac{1}{10}$ milligram of iodine will produce a decided effect upon goitre after 3-4 applications, thus clearly indicating that it is not the iodine *per se* that is effective, but rather the iodine compound.

* Drechsel has reported finding a distinct trace of iodine in the hair of a syphilitic patient treated for a long time with potassium iodide. Centralbl. f. Physiol., Band 9, p. 704.

† Vorkommen von Jod in den Ovarien. Chemisches Centralblatt, 1897, Band 1, p. 608.

‡ Schnitzler und K. Ewald; Ueber das Vorkommen des Thyrojodins im menschlichen Körper. Wiener klin. Wochenschr., 1896, p. 657.

The content of iodine in human thyroids is likewise variable, the determining factor being apparently the locality in which the individual lives. Thus, in 26 adults dying from various causes in Freiburg the average amount of iodine in the thyroid was 0.33 milligram per gram of dry tissue, while in Hamburg the average from 30 adults was 0.83 milligram per gram of dry tissue. In Berlin, average of 11 adults, 1 gram of dry thyroid contained 0.9 milligram of iodine. It should be noted, however, that in the Freiburg cases the average weight of the gland was 8.2 grams with a total content of 2.5 milligrams of iodine. In Berlin, on the other hand, the average weight of the dry gland was 7.4 grams with a total content of 6.6 milligrams of iodine per gland, and in Hamburg the dried gland weighed only 4.6 grams, with 3.83 milligrams of iodine.

Recently Weiss* has reported the results from fifty analyses of thyroids of adults and children in Silesia, the average weight of the dried gland being 7.2 grams and with an average content of 4.04 milligrams of iodine.

From a large number of observations among children and adults in different localities in Germany, Baumann concludes that in Freiburg, where goitre is endemic, the weight of the thyroid is the largest and its content of iodine the lowest, while in Hamburg and Berlin, where goitre is not endemic, the reverse holds good. As a rule, in cases of goitre only minimal and almost always relatively small amounts of iodine are to be found, from which Baumann draws the conclusion that between the iodine-content of the thyroid and the occurrence of goitre there is a certain definite relationship.

I understand, however, that additional results, not yet published, tend to show that in some cases of goitre the content of iodine is far beyond the normal, thus implying the existence of two abnormal conditions: one in which the iodine-content is below, and another in which it is far above the normal. In old age the content of iodine frequently falls to a minimum, apparently in harmony with the degeneration of the gland. The largest amount of iodine is found between the ages of twenty-five and fifty-five.† Many circumstances, however, combine to modify the content of iodine in the thyroids, especially the proximity to the sea-shore with the greater abundance of sea food, etc., and this fact, coupled with the well-

* Ueber den Jodgehalt von Schilddrüsen in Schlesien; Chemisches Central-Blatt, 1897, Band 1, p. 298.

† See Baumann: Ueber das Thyrojodin. Münchener med. Wochenschr., 1896, No. 14.

known circumstance that in the thyroids of some children iodine is wholly wanting (Baumann), and this without any apparent effect upon the activity of the gland, renders one somewhat skeptical as to the real virtue of the iodine. Blum,* however, states that artificial compounds of iodine, with various forms of proteid matter, exert a beneficial influence upon parenchymatous goitre as well as upon the tetanus and myxœdema induced in dogs by thyroidectomy. The iodine in iodothyrin is certainly not active as iodine; the amount is too small, and it may, perhaps, be questioned if the amount of iodine in the thyroid gland can be taken as a measure of the amount of active substance present. In this connection it may be mentioned that animals with the thyroids removed have no power of retaining the iodothyrin administered by mouth or subcutaneouly, the iodine compound appearing in the urine either unaltered or in some modified form (organic).†

To summarize, the thyroid gland manufactures *one* specific substance of marked physiological power—the so-called colloid of Hutchinson—a body which, though containing phosphorus, is not a nucleo-proteid; neither is it allied to mucin. It is peculiar in that it contains iodine. This body, when acted upon by gastric juice or by boiling acids, is split into a proteid and a non-proteid part, the latter containing all of the phosphorus and the larger proportion of the iodine of the original colloid. According to Hutchinson both parts of the colloid are physiologically active, but the non-proteid part, the iodothyrin of Baumann, is unquestionably far more active than the proteid part of the original molecule. This substance is apparently the physiological equivalent of the thyroid gland. Lastly, our history would be incomplete without some reference to the theories of Notkin.‡ This reference, however, may be a brief one, since the theories, though ingenious, are now known to rest upon a false foundation and have no present value.

Concerning the other internal secretions of the body I have little to say, partly owing to lack of time and partly because there is very little definite chemico-physiological knowledge at our disposal. Our knowledge has not as yet advanced sufficiently to admit of

* Ueber Halogeneiweissderivate und ihr physiologisches Verhalten. Münchener med. Wochenschr., 49, 1099.

† Baumann und Goldmann, loc. cit. See also H. und M. Frenkel. Jod im Harn nach Einnahme von Thyreodintabletten. Berliner klin. Wochenschr., xxxiii, 37, p. 827.

‡ Zur Schilddrüsen-Physiologie. Virchows Archiv., Band 144. Supplementheft, p. 224. This paper contains a very full bibliography. Notkin's theories are well combatted by Hutchinson, Journal of Physiol., Vol. 20, p. 490.

making dogmatic statements regarding the exact chemical nature of the active principles present in the adrenals, testicles, ovaries, pancreas, pituitary body, etc., or of the exact action of extracts of these glands upon the metabolic phenomena of the body. Allow me to say, however, in reference to the adrenals, that there is some evidence of the existence of two distinct physiologically active substances, one insoluble in 90 per cent. alcohol, possibly the sphygmogenin of Fränkel, which increases blood-pressure, while the other, which is readily soluble in alcohol, causes paralysis of the heart and muscles and death by suffocation.* In this connection it will be remembered that Oliver and Schäfer† have shown that the active principle (or principles) is non-volatile and that its activity is not destroyed by mineral acids or gastric digestion, while alkalies gradually diminish it. According to Marino-Zuco,‡ the toxic action is due to the presence of neurin glycerophosphate. There are also some grounds for believing a brenzcatechin-like body to be present,§ which may exert some physiological action. Lastly, in extracts of the testis a peculiar nitrogenous body has been detected, free from oxygen, known as spermin and which is claimed by Poehl‖ to have a marked influence upon metabolism and to act as a true physiological stimulus. Further discussion of these points at the present time, however, would have little value.

* See S. Fränkel: Beiträge zur Physiologie und physiologischen Chemie der Nebenniere. Centralbl. f. Physiol., Band 10, p. 486. Du Bois: Note préliminaire sur l'action des extraits de capsules surrénales C. R. Soc. de Biol., 1896, p. 14.

† The physiological effects of extracts of the suprarenal capsules. Journal of Physiol., Vol. 18, p. 370. See also B. Moore: On the Chemical Nature of the physiologically active substance occurring in the suprarenal gland. Ibid., Vol. 17. Proc. Physiol. Soc., March, 1895.

‡ Archiv. d. Biol. Ital., Tome 10, p. 325.

§ Brunner: Chem. Centralblatt., 1892, I., p. 758. Mühlmann: Deutsche Med. Wochenschr., 1896, No. 26.

‖ Compt. rendu., Tome 115, p. 129. Zeitschr. f. Klin. Med., Band 26, p. 133. Centralbl. f. d. Med. Wissensch., 1892, p. 950. See also Bubis: Sperminum Poehl in chemischer, physiologischer und therapeutischer Beziehung. Ibid., 1894, p. 703.

INTERNAL SECRETIONS CONSIDERED IN THEIR PHYSIOLOGICAL, PATHOLOGICAL AND CLINICAL ASPECTS.

The Internal Secretory Activity of Glands in Relation to the Pathological Anatomy of Sundry Morbid Conditions—Diabetes, Addison's Disease, Myxœdema, Cretinism, Graves' Disease and Acromegaly.

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To remove an organ and study the effects of the operation is clearly an exercise in experimental pathology and only secondarily and indirectly a physiological investigation, while the greater the precision with which the course and symptoms of any morbid condition are studied, the more the study becomes a matter of science, a matter of pathology rather than of medicine. In other words, asked as a pathologist to enter into this discussion, I find that all other participants have trespassed into pathological territory. This is one of the penalties of sure advance in our common subject: the pathology of yesterday becomes the medicine of to-day, and I might add, the medicine of to-day yields place to the surgery of to-morrow. But this being the case, so as not to reiterate, I am impelled to make my contribution to this discussion a *resumé* of the results obtained in a branch of pathology which others are not likely to dwell upon. It is in many respects an unsatisfactory branch—a branch capable of testing rather than of originating any theory. I refer to morbid anatomy.

I propose, therefore, during the next few minutes, to lay before you what may be gleaned from the post-mortem room bearing upon this subject of internal secretion. But first it is necessary to call your attention to the very narrow limits of the information to be gained from a study of the gross and fine anatomy of diseased organs in this connection.

Morbid anatomy alone can tell us singularly little concerning alterations in function. The existence of lesions recognizable to

the naked eye or under the microscope may support conclusions reached by other means. It can do little more. We know from experiment that three-quarters of the liver, for example, may be removed from the healthy animal with no pronounced disturbance of the bodily functions, that whenever one-fifth or less of the pancreas is left in the dog it may be weeks before diabetes shows itself, that only when fifteen-sixteenths of the thyroid are removed may the dog succumb. In this enormous reserve of material and force may truly be said to lie the secret of the continued existence of living beings. Thus the mere fact that the greater part of an organ is found wanting by the anatomists, or replaced by tissue of another nature, is not in itself absolute evidence that what remains of the organ is functionless or incapable of meeting the needs of the organism. So long as any considerable number of what may be termed the specific cells of an organ are to be determined, we must proceed very cautiously in our reasoning; only when the destruction is absolute or nearly so are we on sure ground. Contrariwise, if the cells of an organ appear very slightly altered, while we are acustomed to argue that there has been but little disturbance of function, it is questionable whether we are justified in this opinion. So also if an organ like the thyroid be markedly hypertrophied, that is not in itself proof positive that there is accompanying increased activity and increased internal secretion. In the thyroid, for instance, the boundary line between pure hypertrophy and overgrowth of adenomatous nature is peculiarly vague. It may very possibly be that a simple adenoma of a ductless gland continues to supply an internal secretion; it is difficult to imagine that gland structure of almost perfect type can be present in the body without affecting the body at large.* Nevertheless we have no conclusive evidence that this is the case; hence, it is only after most exact and extensive histological study that we can advance any very secure arguments upon the existence of apparent simple hypertrophy, more especially of the ductless glands. The force of this statement will be seen when we come to discuss the bearing of disease of the hypophysis cerebri.

Another matter that has to be taken into account, one that has until now received scant attention, is the existence of vicarious

*It is noteworthy how frequently, in attempting to co-ordinate the anatomical data in the class of disease now before us, we are brought to regard the possibility—nay, probability—that neoplasms are not functionless (as we are too apt to consider them), but afford, it may be, an abundant, internal secretion.

activity. Because one organ is seriously diseased it does not follow that the organism as a whole exhibits disturbances commensurate with the lesions in that organ; other parts may vicariously fulfil its functions. We have the well known example of total extirpation of so important an organ as the spleen being succeeded for years by good health. Here, presumably, the lymph-glandular tissue in general takes over the functions of the absent organ. There is the compensatory development of the parathyroids in athyrea, and further, the frequent, but not constant co-existence of atrophic disease of the thyroid and hypertrophy of the pituitary to which Boyce and Beadles (1) have more especially called attention. Similarly and curiously we meet with frequent persistence or enlargement of the thymus when either the thyroid or the pituitary body is the seat of disease. Thus not only is it a matter of peculiar difficulty in that class of diseases, which to-day we have specially to discuss, for the anatomist to determine which of the ductless glands is primarily and which secondarily affected, but the added difficulty besets us, and where the vicarious function is perfect and compensation is complete we may, in the apparently unaffected individual, meet with lesions of an organ—the thyroid for instance —of the same nature as, and every whit as extensive as, the lesions in well marked cases of those special forms of general disease which we are inclined to regard as the direct outcome of disease of that organ.

Time after time this co-existence of apparently identical lesions in cases of relative health and pronounced disease places us in a quandary, time after time we find ourselves groping vainly in a maze of facts which seem to point in all directions of the compass. And when the facts appear flatly to contradict each other one cause of discrepancy must be this vicarious activity.

Yet another consideration, seriously weighing upon the morbid anatomist, is that two opposite processes may produce a similar symptomatology, one that he can recognize, another that he cannot. If the glands afford an internal secretion entering the lymph and so eventually circulating through the system, we know that the ultimate use of the secretion must be to effect a chemical transformation of some substance or substances in some other part or parts of the system. There are thus four possible conditions: (1) production of an insufficient amount of internal secretion of any gland in consequence of disease of that gland, and (2) the assimi-

lation or production of an excess of that substance which normally is acted upon and transformed by the internal secretion in question. In both of these first two cases there will be a heaping up in the system of the substance; in both there may be the same train of symptoms. In the one the gland or glands may show the clearest signs of disease; in the other they may appear normal. The morbid anatomist may in time discover collateral disturbances distinguishing these two states; at present he cannot adequately. In one case of diabetes he finds the pancreas unaffected, in the next it is extensively diseased. Unaided by experimental pathology, he is quite incapable of determining the important *rôle* played by this organ in regulating the sugar supply of the organism and in the production of diabetes. Similarly there may be an accumulation of the internal secretion, either due to (3) hypertrophy of a gland, or (4) not associated with recognizable glandular change.

In short, gentleman, I fear that I stand before you as a kind of reversed, contrary Balaam. Summoned to bless—to illumine this discussion—I can only curse and can but point out to you the darkness that is upon the face of the deep. But happily there is this to be said to the credit of the morbid anatomist, that the demonstration of this darkness is of the highest value as indicating the lacunæ in our knowledge and suggesting the various factors that have to be taken into consideration, and carefully studied, in order that we may gain a comprehensive knowledge of this intensely interesting and valuable subject of internal secretion and glandular function.

And then, perhaps, things are not quite so black as here painted. While it may be that I am overbold, it may also be that this darkness but precedes the dawn; that facts which seem so flatly to contradict each other can, in the growing light of experimental pathology, already be seen to range themselves in an orderly manner. Accepting the postulates, first, that the glands of the body afford an internal secretion capable of acting upon and transposing some substance or substances produced or assimilated by other regions of the body, and, second that, proceeding with due caution, we can utilize the results of anatomical and histological studies, then, applying the considerations which I have just urged, we must recognize the possible existence of three orders of conditions, each order being capable of further subdivision into two well marked groups.

It would seem that we have to deal with:

Changes Associated with Symptoms of Disease.

I. Glandular Inadequacy.—Excess of substance acted upon by the internal secretion of a gland, without due compensation.

(1.) Absolute. Altered condition of gland leading to diminished activity and diminished internal secretion.

(2.) Relative. No disease or alteration of gland, but excessive production or assimilation of the substance acted upon by the internal secretion.

II. Glandular Over-Activity.—Excess of internal secretion without compensation.

(1.) Absolute. Altered condition of gland leading to increased activity and increased pouring out of internal secretion.

(2.) Relative. No disease or alteration of gland, but diminished production or assimilation of the substance acted upon by the internal secretion of that gland.

Changes Unaccompanied by Symptoms of Disease.

III. Compensation.—

(1.) Altered condition of gland leading to (*a*) increase or (*b*) diminution of internal secretion, with due compensation.

(2.) (*a*) Increased or (*b*) diminished production or assimilation of substance acted upon by internal secretions, with due compensation.

Let me here emphasize the fact that I do not pretend that this table includes every possible condition leading to local or general disturbance of these glands affording an internal secretion, and leading to the symptoms most often associated with disease of these glands. For example, we know from experiments with phloridzin that glycosuria may, among other things, be the result, not so much of increased production of sugar as of increased removal of this body through the kidneys. Such cases are not embraced in this table. Again, what I may term compound cases, as, for instance, of glandular inadequacy, in part from disease, in part from increased production of the substance acted upon by the secretions, are presented only by implication. All I urge is, that this table, conforming with what experiment has shown may occur, may very possibly be utilized to explain the apparently contradictory revelations of the post-mortem room. Can it be so utilized? While I will not say that in connection with every gland we shall find evidence of the existence of each of the three main orders of the above table, I must acknowledge that the acceptance of the considerations here

brought forward aids wonderfully in explaining facts otherwise inexplicable and chaotic.

I would now proceed rapidly to review those conditions, local and general, concerning which we have already a modicum of knowledge and which fall within the scope of to-day's discussion.

THE PANCREAS AND DIABETES.

Let me in the first place take into consideration lesions of the pancreas and their relationship to diabetes. Much more than a century has passed since attention was first called to the pronounced changes to be seen in the pancreas in some cases of diabetes. We all know that not until 1889, when Von Mering and Minkowski in Germany, and de Dominicis in Italy, published the results of their researches, did the belief in the existence of a pancreatic diabetes begin to become generalized, but even at the present moment the fact that two cases, closely resembling each other clinically, may post-mortem show, the one extensive pancreatic disturbance, the other an apparently healthy pancreas, creates great confusion.

What then can be gathered so far as to the relative frequency and the nature of the lesions of the pancreas which may be associated with diabetes?

We have at least three careful studies upon this subject, those of Hansemann (2), Williamson (3) and Dieckhoff (4), and all demonstrate that three conditions may be distinguished: (1) very extensive pancreatic disease with associated diabetes; (2) very extensive pancreatic disease without diabetes; (3) diabetes unassociated with recognizable pancreatic disease. Hansemann, from a careful investigation of the records of the Pathological Institute and the Augusta Hospital at Berlin, found that the first condition (of pancreatic disease with diabetes) is more common than the two others combined. It may be said that in Berlin the consumption of much beer predisposes to the pancreatic form of the disease; it may be that the material upon which Hansemann worked was imperfect to this extent, that full care was not taken to distinguish between extensive and extreme destruction of the pancreatic tissue; but it will, I think, be the experience here, as it was that of Williamson in England, and Dieckhoff in Rostock, that advanced pancreatic disease, associated and unassociated with diabetes, are to be encountered the one but little more frequently than the other.

This much, however, stands out very prominently, that where in diabetes the pancreas is found affected, the morbid process within

the gland is some one or other form of atrophy and destruction of the gland substance. Most commonly it is a form of periacinous fibrosis, originating it would seem secondarily to arterio-sclerosis, in which with thickening of the arterial walls there is malnutrition of the gland cells, atrophy and, what I have elsewhere termed, replacement fibrosis. Other forms of atrophy and fibrosis have not infrequently been observed—simply atrophy, congenital syphilitic fibrosis, obstruction of the ducts with calculi, dilatation of the ducts and atrophy of the gland tissue, scirrhous cancer of the pancreas, and I have found recorded five cases of necrosis, or hæmorrhagic necrosis (two by Fitz and a third, a case under Drs. Bell and Finley, in my own experience at the Montreal General Hospital).

There can, therefore, be no question that the pancreatic lesions found in some cases of diabetes are such that there must be a marked diminution in the secretory activity of the gland. To this extent, in this one class of cases the results of autopsies are clearly in accord with the results of experiments. We have here examples of glandular inadequacy brought about by altered condition of the pancreas leading to diminution of internal secretion.

Examples of diabetes unassociated with disease of the pancreas are so well known that I need but refer to them. While such are difficult to explain from purely anatomical considerations, the fact that they are found, and found relatively frequently is, in itself, an evidence that glycosuria is of at least a two-fold origin. That they are found is in conformity with the results of experiments, experiments which, on the whole, must be regarded as proving that there can be heaping up of sugar in the organism beyond the transforming power of the pancreatic internal secretion, or otherwise an incomplete burning up of the sugar. If this heaping up be in general due to increased glycogenesis, increased production of sugar, we should expect to find some evidence of increased activity of some glycogenetic organ, and here the recent researches of Glénard (5) and Triboulet (6) tend to show that this may be the case. Contrary to the older and generally accepted teaching, Glénard finds that clinically in over sixty per cent. of diabetics, there is evidence of some hepatic enlargement. Anatomically he finds that three conditions may be recognized, each possibly a stage in one morbid process, namely, hyperæmia, general cellular hypertrophy (hyperplasia) and hypertrophy with cirrhosis (hypertrophic cirrhosis). Thus while I will not say that anatomical considerations prove the existence of my second sub-order in this connection, I

must point out that the existence of this class of cases of diabetes without adequate recognizable pancreatic disturbance, is best explained on the supposition that there may be excessive production or assimilation of sugar with accompanying relative pancreatic inadequacy.

There is yet a third group of cases to be considered, that of extensive atrophic disease of the pancreas without diabetes. Here we have to proceed cautiously in our reasoning. As I have already indicated, Sandmeyer (7) has found that if only one-fifth to one-ninth of the organ be left in the dog, it may be months before sugar appears in appreciable quantities in the urine. Vaughan Harley (8) gives an even smaller amount, namely, one-fifteenth, but evidently he refers not to the eventual development of diabetes, but to its onset within a few hours. We can thus state that so long as from one-ninth to one-fifteenth of the glandular tissue of the organ is functional, for so long glycosuria need not manifest itself in the dog. There is no valid reason why we should not apply these facts to the human being. Hence so long as a very small proportion of fairly healthy gland tissue is left, we have a satisfactory explanation why diabetes should not show itself, even though the major portion of the pancreas exhibits fibroids and atrophic or neoplastic changes. There are, however, aspects of that subject not capable of so simple an explanation. I remember my friend, Dr. H. D. Rolleston, of St. George's Hospital, showing to me a series of sections of the fibroid pancreas taken from both diabetic and non-diabetic cases, from which the only conclusion to be reached was that a given extent of fibrosis might or might not be associated with diabetes. Again, Hansemann has called attention to cases of complete replacement of normal pancreas by a diffuse cancerous infiltration without the development of diabetes. He seeks to explain these by the hypothesis already indicated, that the cells of a primary new growth of a ductless gland may continue to furnish an internal secretion. This may or may not be the case. Where there is primary cancer of the hepatic parenchyma, the new growth in the liver may be devoid of bile; the secondary growths are without exception free from bile. A more simple explanation of these and other examples of complete or almost complete destruction of the pancreatic glandular tissue is that of compensation, whether by vicarious function of Brunner's and other glands (the duodenal glands have frequently been found enlarged) or by diminished assimilation or production of sugar. However I will not venture to say that Hansemann's hypothesis may not, after all, be the true solution.

THE SUPRARENAL BODIES AND ADDISON'S DISEASE.

We meet with an identical series of cases in connection with another organ in which experimentally the existence of an internal secretion has been fully demonstrated. We may have (1) Addison's disease associated with disease of the suprarenal bodies, (2) Addison's disease with intact suprarenals, and (3) extensive, if not complete, destruction of the suprarenal bodies without the symptoms of Addison's disease.

Here, as with the pancreas in diabetes, the affection of the gland in Addison's is some form of atrophy or destruction of the specific gland tissue. Most frequently, I need scarce say, the change is tuberculous and necrobiotic, resulting in the disappearance of the gland tissue and its replacement by caseous material. But cases are on record of simple atrophy, hæmorrhagic necrosis and malignant growth of the bodies associated with or leading to all the symptoms of Addison's disease. In the vast majority of cases both glands are affected, but cases are on record (I have come across one such) where only one of the bodies has been the seat of recognizable disease. Of the three conditions above mentioned the most frequent found is the association of the disease with complete or almost complete destruction of the gland. So frequent is the association that the attempts to explain away the other two rare states of Addison's disease with intact suprarenal bodies and suprarenal disease without the Addisonian symptoms, have been almost painful in their ingenuity. Yet undoubtedly well authenticated cases are on record of both of these conditions.

We have in this connection singularly full statistical collections of cases. That of Lewin (9) is well known; he collected accounts of 285 cases, of which 211 showed caseous lesions of the suprarenals (74%). Gilman Thompson (10) found an even greater proportion of either primary or secondary tuberculosis (80%); in the remaining 20 per cent. there were either other forms of atrophic disease or absence of recognizable disturbance.

The existence of cases of Addison's disease without obvious disease of the suprarenal is generally acknowledged. Lewin found that as many as 12% of his cases were of this type. The explanation generally given is that in these there had been alterations in the neighbouring semilunar ganglia and abdominal sympathetics. Certainly, disturbance of the nervous system, and especially of the sympathetics, does lead to pigmentation of the skin. We see this in cases of hysteria and again in Graves' disease, in which from

whatever cause (I shall speak of this later) we have most marked nervous changes, but I must confess that I feel some little impatience towards the upholders of this semilunar ganglion theory of Addison's disease, for scarce two of them describe the same order of lesions. Most of the changes described would appear to be quite common in the adult dying from other causes; thus Hale White (11) found that examining 33 semilunar ganglia removed indiscriminately, if we leave out of account 3 perfectly normal taken from young children, 24, or 80 per cent. of the remainder, exhibited more or less extensive degenerative changes with frequent presence of granular masses of pigment. Dixon Mann (12) also, making a careful comparative study of the abdominal sympathetics and semilunar ganglia from two cases of the disease and from the unaffected individual, came to a like conclusion. He found them not more affected than are those of other individuals. Under the circumstances, therefore, I see no valid reason why cases in which the bodies are found apparently unaffected may not, in the light of our present knowledge, be most satisfactorily classed as possible examples of relative glandular inadequacy of the second class. This suggestion may to some appear revolutionary; but let me reiterate my main argument: We acknowledge that glands like the suprarenals produce an internal secretion: we must inevitably admit that the function of such secretion is to affect a chemical transformation of some substance or substances distributed in other parts of the body: we must admit that when, for example, the suprarenal bodies are diseased, or removed, some at least, of the symptoms that follow are due to the absence of the internal secretion, or, in other words, are due to the accumulation in the system of the substance or substances acted upon by the internal secretion. The same symptoms must be produced whatever the cause of the accumulation of the substance or substances, whether by diminution of the internal secretion or by excessive production or assimilation of the aforesaid substance or substances. When, therefore, a morbid condition, such as diabetes or Addison's disease, which may be caused by destruction of a gland, is found to exist without recognizable disease of that gland, a very possible explanation of the condition is what I have termed relative glandular inadequacy due to excessive production or assimilation of the substance acted upon by the internal secretion. I would but ask you clearly to picture this, that in diabetes and Addison's disease it is not the internal secretion that causes the symptoms, but, if experimental data are to

be trusted, the lack of the same—and that this lack may be absolute or relative.

I am far from suggesting that the whole corpus of symptoms will be the same in both conditions. Thus as Harley and others have pointed out, where the pancreas is atrophied there are profound digestive disturbances not necessarily accompanying diabetes unassociated with pancreatic disease. But I am inclined to think that the cardinal symptoms in both will closely resemble each other.

A few words only are necessary concerning affections of the suprarenal bodies without symptoms of Addison's disease. If bronzing be required as the one essential symptom, then cases of tuberculous disease of the suprarenal without "Addison's" are fairly frequent. Addison himself noted this condition. We must however, it seems to me, acknowledge with Chvostek (13) and numerous previous observers, that bronzing is but one of a group of symptoms, even though we be not prepared to accept Bedford Fenwick's (14) suggestion that bronzing is especially connected with disease of the cortical layer. Leaving this category out of consideration, cases of extensive atrophic or neoplastic disturbance of both suprarenals without Addison's disease are few in number, far fewer than the cases of extensive pancreatic disease without diabetes, and in general the descriptions given are not sufficiently exact to be relied upon. Nevertheless they exist. Greenhow (15) apparently met with a case of almost complete atrophy without symptoms, and, in 1050 autopsies upon subjects dying from diseases other than Addison's, Rolleston (16) met with an example of caseation of the right and atrophy of the left suprarenal and with three cases (under the age of forty-five) in which both were peculiarly small. All these were without symptoms intra-vitam. There are more frequent examples recorded of cancerous growth destroying both bodies without noticeable symptoms. There is a possibility that the new growth here was so rapid and so recent that symptoms had not time to develop. In the atrophic and tubercular cases it is not so easy to accept this explanation. Therefore, I am inclined to believe that compensation may occasionally manifest itself in man as it does occasionally in animals which have suffered complete ablation of both organs.

THE THYROID GLAND AND MYXŒDEMA.

I have already approached the limits of the time allotted to me and there is yet for me to pass in review the gland and its affections,

which in this connection have created the most general interest. I refer to the thyroid and to the conditions of myxœdema, cretinism and exophthalmic goitre.

From an anatomical point of view there is little for me to say in elucidation of the pathology of myxœdema beyond the one all-important statement that, with very rare exceptions, there is discoverable a well marked atrophy of the thyroid. About this all pathologists are agreed. In the majority of cases the atrophy is peculiarly extensive, the specific cells of the gland being replaced by fibrous tissue: in some it is not so far advanced, and areas may be found, not merely of degenerated remains of the vesicular epithelium, but of vesicles which by the superabundant proliferation of their epithelium would seem to be undergoing a compensatory hypertrophy. Yet where these are present they are localized and few in number; the main mass of the organ shows atrophy. A few cases only are on record, like that of Gulliver (17), where there has been a cancerous metamorphosis or replacement of the parenchyma.

That in these cases the myxœdema is associated with diminished internal secretion of the gland is, I need scarce say, substantiated by the good effects of treatment by thyroid extract or thyroid feeding.

It must next be asked whether myxœdema can show itself with apparently intact thyroid, *id est*, whether there are any cases which may possibly be explained by excess of the substance or substances acted upon by the internal secretion of the gland. The literature is peculiarly silent upon this point. I can find no example of autopsies upon cases diagnosed clinically as myxœdema in which the gland was found normal, or but little affected. Possibly my search was not sufficiently extensive. I can only recall an autopsy upon a patient of Dr. J. Stewart at the Royal Victoria Hospital, in which I found a large cancerous tumor of the pituitary. Here there had been a myxœdematous swelling of the hands, and of other regions to less extent, without bony overgrowth, and no change was found in the thyroid. The condition, however, was not sufficiently advanced to deter Dr. Stewart from diagnosing tumor of the hypophysis. A somewhat parallel case (of apparent atrophy of the pituitary), in which the symptoms of myxœdema were more marked, is recorded by Codd (18), but the anatomical details are given very briefly. Similarly we possess no exact records of atrophic disease of the glands unassociated with myxœdema. I can only point out that it is not uncommon in the aged, who show no signs that can properly be regarded as myxœdema—unless

senility itself be regarded as such—to find a condition of very extensive chronic interstitial thyroiditis (as it may be termed) with arterio-sclerosis, calcification and hyaline changes, with retrograde or pseudo-embryonic type of vesicles. I have come across more than one case of this nature. There can be no doubt that here the secretory activity of the gland tissue must be very greatly reduced. If, however, we turn to cases in which by surgical means the equivalent of complete atrophy, namely, complete thyroidectomy, has been attained, we then possess abundant evidence that the thyroid proper may be absent without myxœdema necessarily intervening, and almost as abundant evidence from the more recent researches that the absence of symptoms is connected with vicarious activity on the part of other organs, and especially of the parathyroids. These may be regarded either as true accessory thyroid tissue, or as distinct organs, according to the point of view of the individual. Certainly when the thyroid is functional they do not acquire the full characters of thyroid tissue, but similarly there are often within the healthy organ scattered areas of embryonal tissue. This can be said with precision, that they are independent masses of tissue, apparently most closely related to the thyroid, which are at times capable of development to, or towards, the adult type of the gland, and of assuming vicarious functions. In like manner the pituitary body can at times undergo very definite compensatory enlargement. This was first demonstrated experimentally by Rogowitsch (19), while Boyce and Beadles more especially have added to our knowledge of its enlargement in cases of myxœdema, cretinism and cachexia thyreopriva.

An interesting point in this connection, to which attention has been drawn by Rogowitsch, is that the rabbit, from which the thyroid can be removed with impunity, has a pituitary body relatively five times as large as that of the dog, in which ablation of the thyroids leads rapidly to symptoms of acute athyrea; or more correctly, the relationship of thyroid to pituitary is 3 to 1 in the former, 15 to 1 in the latter animal.

On the whole, therefore, anatomical data in connection with myxœdema and cachexia thyreopriva support and are capable of explanation by this doctrine, that where glands afford an internal secretion, the development or non-development of symptoms of disease depends primarily upon the relative amount of internal secretion produced and of the substance or substances acted upon by the same.

CRETINISM.

Cretinism presents a far more complicated histological picture—so complicated that Bircher (20) argues with very considerable force that "cretinic degeneration, as also dwarfism and chondrodystrophia fœtalis hypoplastica have no ætiological connection with the functions of the thyroid." Bircher, however, fails to recognize that if we accept the existence of an internal secretion, we must also admit the presence of substances upon which that acts, and he cannot see that widely contrasted anatomical conditions may lead to the same train of symptoms. We must, I think, abide by the experimental and clinical evidence that removal of the thyroid in the young leads to a condition indistinguishable from cretinism. This being so, we find that in some few cases of typical cretinism the thyroid is completely absent, in a large number it is small, in a yet larger number, according to Von Eiselberg (21) and Kocher (22) there is a goîtrous condition present, while according to Bircher the goîtres may be of all possible forms, from simple hyperplastic through soft (parenchymatous) and cystic to fibroid. The only point clearly to be made out from Bircher's very destructive criticism is that while in several cases the thyroid has been found of normal size, apparently no case exists in which by microscopical observation it has been found of normal structure. Considering the amount of material he brings forward this is rather remarkable. I further gather that his statements as to the frequency of the various forms of goître are based upon examination of the living and not upon the post-mortem or surgical material. This seriously weakens his case. Beyond this I will not venture to travel. Bircher's statements require to be dealt with by one in authority, and I await with interest Dr. Osler's presentation of the matter.

EXOPHTHALMIC GOITRE.

I will now briefly refer to the condition which presents a series of symptoms so remarkably contrasted with myxœdema—which also anatomically presents an equal contrast. There is to be found in exophthalmic goître, as Greenfield (23) has shown, and as is now generally accepted, a characteristic hyperplasia of the thyroid parenchyma, complicated, it may be in later stages, by increased fibrosis. The one question of immediate concern here, is whether from this we can safely deduce that there is accompanying increased internal

secretion. As I have already hinted, I do not think that from anatomical considerations alone we can safely make this deduction. There is, however, an important fact in favor of such deduction, namely, the strong likeness between the primary glandular changes in Graves' disease and those described by Halsted (24) and others as occurring in the compensatory hyperplasia of the thyroid after removal of large portions of the gland; and if, together with the anatomical changes, we consider the favorable effects which so often follow removal or destruction of the hypertrophied gland in this disease or diminution in the blood supply of portions of the same—of operations which must lessen the internal secretion—it is difficult to arrive at any other conclusion than that in exophthalmic goître there is increased internal secretion, and that this plays a singularly important part in the development of the symptoms. Whether this be primary or secondary to lesions of the central nervous system—of the restiform bodies for example—our present anatomical data are insufficient to decide, as again they are incapable of deciding whether the increased secretion is altered or unaltered in quality. I may here note that, as Joffroy and Achard (25) have indicated, the symptoms of parenchymatous and adenomatous goître are at times curiously allied to those of exophthalmic goître. Indeed, together with Vanderwelde and le Bœuf, they hold, I think without due cause, that there is nothing anatomical to distinguish the one condition from the other. That the one condition may lead to the other is a matter of clinical experience. As Dr. Shepherd has pointed out to me, extirpation of the goîtrous nodules or cysts leads to the almost immediate amelioration of the symptoms, more especially those of a nervous character.

The development of exophthalmic goître without hyperplastic alteration of the thyroid is a matter concerning which there is little anatomical evidence. I find one case recorded by Joffroy and Achard in which the gland was of normal size and, while not normal histologically, presenting nevertheless a series of changes wholly distinct from Greenfield's classic description. The vesicles, instead of being small and corrugated, were enormously distended; instead of absence there was abundance of colloid material; in place of a columnar and proliferating epithelium, the lining cells were flattened. Not a few believe in the existence of Graves' disease without goître. Among recent writers Buschan (26) especially holds this view, but save in the above case I cannot find anatomical substantiation for the opinion. Clinically Graves' disease without enlarged thyroid has very frequently been noted; in some cases

enlargement supervenes, in others it does not, but there may well be increased activity of the gland without marked enlargement. All that can be said at present from this evidence is that apparently the condition does occur. So also evidence as to the occurrence of marked hyperplasia and presumably increased secretion without symptoms is not so full and precise as could be wished. I can only point out that if adenomatous nodules in the thyroid produce any internal secretion, then, while many cases of adenomatous goître show a train of symptoms somewhat allied to exophthalmic goître, and while a few cases pass on to undoubted Graves' disease, many on the contrary appear to last for years without symptoms. And in autopsies upon those dying from diseases, other than exophthalmic goître, we find a wide variation in the condition of the thyroid, from atrophy on the one hand to a condition not far removed from what Greenfield and others describe in association with exophthalmic goître.

Altogether, therefore, while not prepared, from general as from anatomical considerations, to state positively that exophthalmic goître is in all cases primarily due to increased thyroid secretion, I cannot but admit upon the whole that the facts can be best reconciled by assuming the existence of increase in glandular activity, whether absolute or relative.

THE PITUITARY BODY AND ACROMEGALY.

Finally some few words must be said concerning that strange collection of symptoms and anatomical changes to which Marie has given the name of acromegaly. Yearly it has become more clearly recognized that the term indicates a definite disease, although there is a liability towards confusion with gigantism on the one hand, and on the other with the remarkable overgrowth of bone in certain cases of chronic disease (mainly of the lung), which again Marie was the first to group together under the title—voluminous, and in other respects unsatisfactory—of hypertrophic pulmonary osteoarthropathy.

Here again the remarkable trio of conditions forces itself upon our notice; there may be acromegaly with disease of the pituitary, acromegaly with apparently unaffected pituitary and extensive disease of the pituitary without acromegaly. Where there is acromegaly, there in by far the greater number of cases the glandular portion of the body is diseased. It is true that the condition is

rare. Between 1890 and the present time less than thirty affected subjects have undergone post-mortem examinations. Leaving aside from lack of time sundry interesting observations upon the state of the thyroid and thymus, I may say that this one gland alone—the pituitary—has been repeatedly found altered, the alteration being especially in connection with its anterior or glandular portion. Out of 24 necropsies upon cases stated to be acromegaly, Tamburini (27), the latest collector, finds that in 17, or over 70 per cent., the pituitary has been found diseased. The remaining 7 are subjected by Tamburini to severe criticism, with the result that he rejects 2 on the ground that the condition had only been recognized clinically for a few months and no microscopical examination had been made. He presumes that time had not been sufficient for the development of naked eye changes. Three other cases he holds to have been osteoarthropathy. There remain two which he could not definitely reject and consequently classified as doubtful. So far as I can follow Tamburini he is strongly of opinion that morbid changes in the hypophysis cerebri are essential to acromegaly. The majority of observers do not accept this extreme view, and with them I am inclined to believe that here, as certainly obtains in diabetes and Addison's disease, there may be typical symptoms without recognizable involvement of the pituitary.

But granting this much, that in the majority of instances the gland is diseased, it is difficult to advance much further, for there is a curious discord concerning the exact nature of the alterations in the pituitary body. In about one half of the cases hypertrophy of the organ is described. Stroebe (28), Tamburini, Boltz (29) and others of later date conclude that the change is adenomatous, Marino (30), Dallemagne (31) and Gauthier (32) describe a peculiar cystic degeneration, Boyce and Beadles a cystadenoma, while in another of Dallemagne's cases and in Wolf's (33) there was clearly sarcoma, and in Bury's a "glioma." What are we to conclude? Is acromegaly accompanied by an increased pouring out of internal secretion, or the reverse? Mere hypertrophy and possibly adenomatous overgrowth might lead to increase, but surely degenerative changes and sarcoma can have no such effect.

It is difficult to reason by analogy, and if we attempt this and seek to base any argument upon what occurs in disease of the gland, which anatomically is most closely related to the pituitary—namely, the thyroid—we are led rather to the conclusion that acromegaly must be due to arrest of function of the former. That is to say, there is a certain correspondence between the changes occurring in the

connective tissues in myxœdema and those affecting the bone, and to some extent the subcutaneous connective tissues in acromegaly.

On the other hand, the pituitary is nearly always found enlarged and hypertrophied in general gigantism as distinguished from this localized acromegalic gigantism. It is difficult to reconcile such enlarged hypophysis, while again the contrast may be pointed out between gigantism and cretinic dwarfism. Tamburini, and independently Massolongo (35), have attempted to coördinate the contradictory anatomical discoveries by suggesting that two stages of the disease may be recognized, a first in which the hypophysis undergoes hypertrophy and is in over-action, which may give place to a second in which the hypertrophied tissue either undergoes atrophy or adenomatous or sarcomatous change. The suggestion is seductive, but for the present must be regarded merely as a suggestion.

Briefly, therefore, our knowledge in this connection is miserably inadequate, and experiments have so far been without result. We cannot say whether in acromegaly there is increased or diminished internal secretion. While the change in the pituitary appears often to be primary, we cannot with certainty lay down that this is the case. It has only to be added that if we admit that lesions of the pituitary are associated with acromegaly, we must also admit that compensation can occur, for there is considerably over a score of cases on record of hypertrophy, adenoma and cystadenoma of the organ, all of considerable size and presumably of long duration, which had developed without signs of the disease in question.

Thus to conclude a long discourse, which in justice to the subject I could not well shorten: I have here, gentlemen, followed a single train of thought. Some may find it suggestive, to some it may be so simple as to be specious, so wide in its embrace that its very comprehensiveness is its damnation. I can only point out that which is here written has been already more or less definitely suggested by various writers in this country and elsewhere, in connection with most, if not all, the conditions here discussed, and impress upon you that, if we are prepared to accept the results of experimental research and to believe in the existence of internal secretions, then, inevitably, we must be led to some such views as those brought forward in the course of this paper.

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THE INTERNAL SECRETIONS CONSIDERED IN THEIR PHYSIOLOGICAL, PATHOLOGICAL AND CLINICAL ASPECTS.

On Some Clinical Aspects of the "Internal Secretions."—Nature of the Thyroidal Cachexias, Infantilism, Acromegaly, Graves' Disease.

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The clinical observations which have been made during the past few years, with regard to the cachexias following thyroidal disease, have not greatly changed our views of the fundamental problems of thyroidal pathology, and, interesting as they are in detail,* there are not many of them which have seemed to me appropriate for a brief and general discussion such as this, more especially since they have received such thorough treatment, within the past year, in the monographs of Ewald,† Buschan,‡ and Pel,§ and at the hands of the gentlemen who have preceded me this afternoon in presenting the physiological, pathological, chemical and therapeutical aspects of the subject of the "internal secretions."

I shall, therefore, devote the time at my disposal mainly to the consideration of some of the analogies and contrasts between the effects of disease or removal of the thyroid, the generative organs, and the pituitary body, in the hope of gaining in this way wider conceptions of the nature of the influences at work in one or another special case. For it is obvious that wider conceptions are not only of theoretic interest in this connection, but that without them we shall never penetrate the shroud of mystery which envelops the functions and diseases of these organs.

The researches which have been made hitherto into the pathology and clinical history of the diseases of thyroidal origin,—whether those of thyroidal deficiency, such as myxœdema, or those assumed to be due to excess or alteration of the thyroidal secretions, of which

* Among the most important are the investigations into the metabolism of the thyroidal diseases, but they are not suited for brief analysis.

† Die Erkrankungen des Schilddrüse, Myxœdem, u. Cretinismus. Nothnagel's Spec. Path. u. Therapie, Band 88.

‡ Ueber Myxœdem und Verwandte Zustände. 1896.

§ Volkmann's Samml. Klin. Vorträge, No. 123, 1895.

Graves' disease is the prominent representative,—have been conducted, very properly, with the object of defining such types of disease as were well marked and of determinable etiology, and separating them from the more or less miscellaneous affections with which they might be confounded.

But, important as this analytic method has been and will continue to be, it cannot be regarded as likely to give us all the information that we need. We are rather in the habit of assuming that the removal of large portions of the thyroid does no harm provided it does not cause myxœdema. But the probability is that we shall learn to recognize affections which lie between myxœdema and health, as well as peculiarities of development and disorders of nutrition for which the thyroid is more or less responsible.

The recent experiments of Halsted* have shown that bitches whose thyroids have been partially removed may remain, under ordinary circumstances, in apparently good health, and yet give birth to young that are incapable of sustaining life and have thyroids hypertrophied to ten or twenty times the normal size; and Kocher believes that goitre and cretinism are often inherited, in infected districts, from parents who have no obvious disease of the thyroid but whose thyroidal functions have suffered some kind of impairment.

The very fact that large portions of the thyroid can be removed without exciting myxœdema, inclines one to believe that morbid results occur which we do not yet know how to recognize, for otherwise we should have to assume that its previous bulk was unnecessary, and this in face of the observation (Halsted) that even when the tip of the gland is experimentally injured the whole organ undergoes changes of "hypertrophic" character, leading apparently to an increase of its secreting structure.

It is still a question whether the concurrence of thyroid disease with various dystrophies, not characterized by the typical symptoms of cachexia thyreopriva, as in the interesting cases of subcutaneous fat, hypertrophy, etc., reported by Dercum and Henry,† or in the obesity of hogs [v. Lenz, Deutsche Med. W. schr., 1895, p. 597], or in cases of infantilism, indicates a relationship which is in any degree causal.

*An Experimental Study of the Thyroids of Dogs, etc. Johns Hopkins Hospital Reports, Vol. I.

†Am. Jr. of Med. Sciences, Nov. 1892. Ewald, in his monogram (l. c.) says that he has seen a similar case.

Again, it has been suggested, by Horsley* and by Gley and Ballet,† that we may sometimes find symptoms due to excess or alteration of the thyroid secretion side by side with symptoms of deficiency.

In this way, Horsley thinks, we may best account for the occurrence of dyspnœa (which is so often seen in the case of animals whose thyroids have been removed) in conjunction with the symptoms of Graves' disease.

But if it is entirely conceivable that disorders of nutrition of one or another sort, besides myxœdema, are sometimes due to deficiency of thyroidal secretion, or irritative nervous symptoms, hitherto unrecognized, to its excess or alteration, it is obvious that we have as yet no sufficiently good touchstone to enable us to determine the question in a given case. All that we can do is to define, so far as possible, the directions in which research may safely tend.

Can we use the success or failure of treatment by thyroidal preparations as an indication that a given disease is or is not of thyroidal origin?

The usual assumption seems to be that the success of such treatment, as occasionally in skin diseases, is not a reason for referring the symptoms to this cause. This is probably correct, but we have not an equal right to deny the thyroid origin, or partial origin, of all affections which are not favorably influenced by treatment of this sort. This argument of failure to respond to treatment, has been used as against the view that endemic cretinism is a thyroid affection, and yet there are few persons who now deny that tabes is in some sense due to syphilis, merely because it is not curable by mercury. Each case must be decided on its merits, after taking all the circumstances into consideration, and the argument from the effects of treatment is not conclusive in either sense.

A good deal of doubt is felt by some competent authorities as to whether endemic cretinism should be classed as a thyroid disease, and I wish to consider some of the arguments on either side of the question, even though it is impossible to reach a definite conclusion, because they open up some new points of view which are important in this connection.

The question has, moreover, a special interest for us, since our countryman Munson has shown that goitre, with which in Europe

* Brit. Med. Jr., 1896.

† Semaine méd., 1895, p. 330.

cretinism is closely associated, is endemic among the Indians of the West, especially those living in Montana and Wyoming, on the western slopes of the Rocky Mountains. The writer, an army surgeon stationed at Fort Assiniboine, Montana, has collected reports from among the government physicians at the Indian agencies, covering an Indian population of 147,873 persons. The proportion of goitrous persons reaches, in some tribes, 4.2 per cent. The same mystery shrouds the origin of the disease here as in the mountainous areas of middle Europe. It is obvious that locality is the important factor, but, as Munson shows, the whites in the same locality and drinking the same water are not affected in the same way. They are also less degraded and intermarry less often.

The mineral composition of the drinking-water is given in the paper, but the geological data have not yet been worked out enough to justify a comparison with the conditions existing in Europe.

Cretinism seems to occur but rarely among the Indians; in fact, only one case has been reported. Closer investigations may show this observation to be erroneous, or may explain the cause of the difference existing between the conditions here and those in Switzerland.

The writer concludes that the factor of main importance is that of race, but in view of what the European observations have taught it seems more likely that this is one of the predisposing influences which so strangely complicate the attempt to discover the real cause at work. A similar predisposition exists in heredity. Munson states that the goitrous Indian children are generally born of goitrous parents; but the tendency must have had a beginning independent of direct inheritance, and so we are forced back to a condition of affairs of which the simplest analogue is perhaps afforded by the experiments by Halsted which have been referred to.

The topographic localization of endemic goitre was carefully traced by Bircher* in 1883, and his results seemed to incriminate the drinking-water coming from certain geological formations, not however as deriving any particular chemical constituent from those formations themselves, but as probably taking up some organic substance, the nature of which is wholly unknown. Kocher's observations† do not wholly bear out Bircher's view, that the strata

* Der endemische Kropf u. seine Beziehungen zur Taubstummheit und zum Cretinismus, Basel, 1883. (See the careful summary given by Ewald, l. c.)

† Vorkommen u. Verbreitung des Kropfes in der Canton Bern., 1889. (See also a letter in the Boston Med. Surgical Journal, June 24, 1897.)

from which the dangerous waters come are so limited in kind, and the matter is still *sub judice.*

The consensus of opinion among the best trained observers is, thus, that endemic goitre is caused by an organic poison, but it is still entirely uncertain whether this acts primarily upon the parenchyma of the thyroid, or primarily upon the tissues of other organs. In the latter case, and sometimes even in the former, the disease of the thyroid may be conceived of as resulting from an ineffective effort at neutralization of a tissue poison, or some analogous form of action which, for lack of more definite term, we express in that way. The opinion of Kocher,* formed after many years of observation, that endemic cretinism is of thyroidal origin, and is due to an hereditary influence, even though the parents were free from obvious goitre, is in harmony with this view.

The principal current beliefs as to the nature of endemic cretinism are three. The first assumes that it is essentially identical with infantile myxœdema, and due, like that, to disease of the thyroid,† though only partial disease, since complete removal of the (goitrous) thyroid from a cretin brings on myxœdema. This view is held by able observers, including Kocher. The second assumes that cretinism is independent of thyroidal disease, but is due to the same unknown cause with that which induces endemic goitre. This was the opinion of Virchow, though advanced at a time when the nature of the thyroid functions was unknown, but it has been strongly maintained of late by Bircher, on the basis of his large experience. The third view is that of Buschan (l. c.), who considers that endemic cretinism represents a mixture of myxœdematous cachexia with "degeneracy," due to in-breeding and debased conditions of life.

In the same sense, Bourneville has pointed out that various forms of idiocy may be united with the thyroid cachexia without being in any way related to it.

The arguments bearing on the first two of these views are fairly presented by Ewald, in his monograph (l. c.). He does not commit himself positively to either of them, but believes that true cretinism is probably dependent in part upon thyroid disease, while admitting that the shape and mode of ossification of the cranium, the peculiari-

* l. c.

† An important study of the thyroid (and hypophysis) of cretins, by De Coulon (Virchow's Arch., Bd. 147, S. 53.) has come to my notice since this paper was first prepared. He found evidences of thyroid degeneration, primary or secondary, in all of his cases, including one, of special interest, where the bodily signs of cretinism were present without the usual mental deficiency.

ties of growth, the character of the mental deficiency, the frequent association with deaf-mutism, and other indications, not to speak of the (usual) presence of goitre, militates for the conclusion that this affection deserves to be classified by itself.

The "degeneracy" view of Buschan is reasonable, except that it does not say much that is definite. "Degeneracy" is a broad and vague term. What is it and how shall it be classified, biologically; and under what other circumstances of in-breeding do we meet this particular form of it? Such are the questions which press for an answer.

The "endemic" cretin usually stands much higher than the "sporadic" (myxœdematous) cretin, as regards physical development, but may stand either higher or lower as regards mental capacity. The patients of the latter class, like the myxœdematous patients in general, are apt to exhibit a certain shrewdness which would not at first sight be suspected. In both cases, however, and whether we consider them from the mental or physical side, it may be said that we have to deal with individuals who are degraded, to be sure, but also represent more or less specific types of development.

The same might, no doubt, be said of "degenerates" in general, but, as I have said, the question now before us is whether these special forms of degeneracy are due in any sense to thyroid disease.

As one of the elements for the decision as to the thyroidal origin of cretinism, it is obviously important that we should have as wide conceptions of the nature of the thyroid functions as the facts warrant, and from this point of view, I wish to call attention to certain analogies between the thyroid and other organs, as regards their relation to general nutrition on the one hand and to modified tendencies of growth on the other. It has often been pointed out that each of the different parts of the body may be conceived of as having secretory or excretory functions with relation to all the rest, but the results of the removal of a given organ is greater if, as in the case of the thyroid, it is the only one of its kind, and also if the function which it subserves is of fundamental importance in a chemical sense.

If a comparison be drawn between the effects of removal of the thyroid and those of removal of the generative apparatus, it will appear at first sight that in the former case we induce a deep-seated disorder of general nutrition, and the latter only a specific change in the tendencies of growth. But on a closer view it is, I think, apparent that the deficiencies in either sense are only of degree, not of kind. There are "positive" characters in cretinism and myxœ-

dema which one is liable to lose sight of if he looks at these affections simply as examples of degradation or poisoning, and, conversely, the changes induced by castration, and still more the conditions which arise in connection with defects in the tendencies of development of which the generative function is the centre, bear, in some respects, the aspects of disease.

When any organ of the body is removed two forces are set at work. One of these is the toxic action of various substances, probably not one but many, while the other is the influence attending the effort of the organism to establish a satisfactory readjustment on a new basis. The former of these forces is, in name at least, familiar; it is the latter force that demands closer attention than it has generally received. In the case of pronounced myxœdema the progressive impairment of vitality due to the cachexia overshadows the other tendencies at work, but we shall be more ready to admit that such tendencies may be present after glancing at the kindred results which follow the loss of the generative organs, for these organs represent functions which are likewise of fundamental importance for general nutrition.

In the complex series of changes following castration, which lead to the formation of the eunuch or the ox* (1) we see these efforts at readjustment culminating in the production, not of a poisoned and stunted individual of the original sort, but of a new individual of a different sort, though not always free from disease. If an analogous process takes place in fœtal life or at impregnation, such that a blow is struck at the developmental tendency of which the sexual function is the centre, we see a still more elaborate set of changes induced, and these may lead to *infantilism*, which may, again, be looked on as a successful result up to a certain point, though it is a condition which is liable to become associated with degenerative dystrophies of various kinds.

It is, by the way, conceivable that eunuchism might be cured by following the line of treatment so useful for myxœdema, and giving testicular preparations, and I am surprised that this has never, either in therapeutics or experimentally, been attempted.† It would, however, be hard to believe that the same treatment would work satisfactorily in infantilism.

*The osseous hypertrophy which occurs in this case is of interest in this connection.

† Testicular preparations have been used to a limited extent, and sometimes, it is claimed, with good result, to counteract the ill effects of castration for hypertrophy of the prostate.

The remarkable series of changes which occur when the thyroid gland atrophies or is removed bear so obviously the stamp of disease that the observer slips only too easily into the habit of designating them as "cachetic" and seeking to refer them to the influence of some special poison.

Perhaps no better single name than "cachetic" could be found, and indeed its use seems abundantly justified by the fact that as a rule these changes lead fatally to a progressive degradation of the vital processes. But this degradation is neither so rapidly fatal nor so inevitably progressive as that, for example, which follows removal of the suprarenal capsules or the pancreas, and for certain groups of cases the progression of the cachexia is so slow that we have practically to deal with a stable organism. Such cases are, the milder types of myxœdema, especially myxœdema of infantile origin; perhaps endemic cretinism; and such dystrophies as may be referred in part to thyroid disease.

The effects of castration and the altered tendencies of growth implied by the term "infantilism"* are not called "cachetic," but they are certainly due in part to changes in the composition of the blood, and, as in the case of the athyroidal diseases, it is doubtful if any single term could fully indicate their nature. Darwin and Milne-Edwards refer the results of castration to the action of compensation, the nutritive material set free by the removal of one organ going to increase the available supply of material for other organs. It is probable, however, that the views of these investigators would have been stated differently if they had been familiar with the pathological data now at our command.

The ox, the capon, the eunuch seem, indeed, to have gained in one way as much as they have lost in another—though this could not be positively asserted without studies into their metabolism made with special reference to the toxicity of the blood and urine, and especially in the early stages of the metamorphosis,—but the obesity which so often follows oöphorectomy is perhaps a sign of disease, and the same may be said of the many nervous and mental symptoms which attend castration both in the male and the female.

I have no wish to attempt any new theory to account for the vast

* This term was, according to Meige, first introduced by Brouardel. It indicates a condition, slight degrees of which are familiar to every one, which represents a relative arrest of development at the moment of adolescence or younger. The arrest affects primarily the genital sphere, but involves the "secondary sexual qualities" of both mind and body, and leads to peculiarities of the feminine type.

series of changes in the "secondary sexual attributes" through which, after castration, the male is modified in the direction of the female, and the female* in the direction of the male, or both in the direction of the neuter; but it may be admissible to point out that the influence at work must be in great part humoral in character; and that the chemical character of the secretions must be subject to constant change as the process goes on.

Illustrations of the truth of the former statement are given in the fact that the neutral worker-bee can be made by change of food to develop into the queen,—though according to Milne-Edwards, with diminution of intelligence—and that Hunter found the transplanted spur of the cock-chicken to grow but very slowly on the leg of the hen, while the spur of the hen-chicken transplanted to the cock, grew as rapidly as the normal cock's spur.

The warrant for the statement that one could hardly expect to find a constant chemical condition of the blood and other fluids, be they toxic or not, would seem to be given in the fact that the gross structure is progressively changing in so many respects, and parts are being gained or lost which must have definite functions relatively to the rest of the body as organs of excretion, or modification of the blood.

The series of changes which represent the primary result of castration must act in their turn as provocative causes of a second series of changes, and these will stand in only an indirect relation to the special chemical substances with which the blood became charged in consequence of the first generative disease or mutilation.

It may be assumed that when through the administration of thyroid preparations the process of disentanglement is initiated, as in the treatment of myxœdema, the "poison" which is neutralized is only that which stands at the end of a series and not one which stands behind each and every one of the morbid processes at stake, though how far this explanation is of practical significance is uncertain.

Our knowledge of the group of affections not directly resulting from castration but due to a blow struck, further back, at the developmental tendency of which the sexual function is the central point, has been widened within a few years by the observations of Brouardel, Brissaud† and Meige.‡

* As in birds, and other animals, after cessation of ovulation or after disease of the ovaries, as well as after castration.

† Leçons de la Salpétrière.

‡ L'Anthropologie, 1895, p. 257.

Infantilism. *See page 131.*

The conditions very properly designated by these writers as *infantilism* and *femininism*, slight degrees of which are probably very common, are not only of interest in a general way for the discussion of the "internal secretions," as representing the modifications of the "secondary sexual characters" carried to a further point than after castration, but they are of peculiar interest as being conditions which are often associated with disease of the thyroid.

The removal or atrophy of the thyroid in infancy absolutely checks the development of the genital organs and functions, but it also checks and modifies development in so many other respects that the distinctively sexual results are overshadowed.

In the "infantile," on the other hand, the effects of thyroidal disease, though they must often be present in greater or less degree,* are overshadowed by tendencies of growth of a specialized morphological character.

Infantilism is apt to be associated with other dystrophies and abnormalities, such as dwarfism, gigantism, femininism, muscular dystrophies and impairment of the special senses.

The subject will be made clearer by a brief account of an interesting case which I have recently had an opportunity to examine through the courtesy of Dr. F. C. Shattuck.

The case is that of a young man recently a patient under Dr. Shattuck's care in the Massachusetts General Hospital. (See plate.) He has been blind from birth (with optic nerve atrophy and disseminated choroiditis) and although seventeen years old is a dwarf in size, standing but four feet and four and a half inches high, and is infantile in genital development. There is no hair on the face or pubes.

The skin is rather dry and coarse, and there are pads of fat above the clavicles and spots of vascular congestion on the cheeks, but the hands are not large and no myxœdematous swelling is evident. The abdomen is protuberant, lordosis is present, and he is knock-kneed. His muscles are not only weak,—as they have been since birth—but are distinctly dystrophic and have grown steadily more feeble of late, so that he can not get up from the floor without the aid of his arms, with which he either braces himself against his own thighs or catches hold of his chair. The calves are dense but

* Post-mortem evidence on this point is not abundant, but Meige says that the thyroid is "generally small" in infantilism, and that Brissaud has found it rudimentary in one autopsy.

not large. The gait is slow and waddling. His intelligence is good for ordinary matters, but he is timid, emotional, and childlike in temperament.*

This case is, however, of more interest than as an example of simple infantilism, or infantilism complicated by developmental muscular dystrophy and disease of the eyes, and by diminutive stature and marks of femininism. I fortunately had the opportunity to study the case of the boy's mother and sister, and found in them additional signs of interest from the thyroidal standpoint, in that both of them had goitres of small size, while the sister, like the brother, was almost blind: She, also, had disseminated choroiditis, and, although an intelligent girl and sufficiently well grown in height, with considerable beauty of face, had reached almost fifteen years without ever having menstruated, and showed at least one other stigma of degeneration in that she had but two upper incisor teeth. She presented also some nervous symptoms, such as general excitability, with a tendency to dizziness, faintness and frontal headaches; she had a somewhat rapid pulse (90-96) on the occasion of my two examinations, and a temperature of 99F.

The mother of these children could give no history of earlier cases of either goîtres or myxœdema, but the important fact was developed that the parents were cousins of the first degree.

The natural comment would be, that these are examples of "degeneration" due to in-breeding; but does the much abused term, "degeneration," convey a satisfactory explanation? We know, through the researches of Meige and others, that in infantilism the thyroid as well as the sexual apparatus is usually small, and that infantilism is apt to associate itself with others of these strange disorders of growth; with cretinism and infantile myxœdema. If "degeneration" is the cause, it works, none the less, by striking primarily at the sexual system.

I have dwelt at this length on the subject of infantilism in order to emphasize the view that a close relationship may exist between altered conditions of metabolism due to a specific change in the composition of the blood, such as follows castration performed after birth, and complex disorders of the developmental tendencies in the midst of which the immediate effects of the specific alteration of the blood appear only as one feature of the process. It is legitimate to look for corresponding analogies and relationships among the

* See a recent discussion of infantilism, femininism, etc., by Henri Meige. L'Anthropologie, Nos. 3, 4, 5, 1895.

diseases centering around the thyroid, and perhaps we may find in this way an explanation of endemic cretinism.

Again, the tendency shown by infantilism to associate itself with degenerative disorders not obviously definable as diseases of the secondary sexual attributes, is possibly analogous to the tendency which unites certain dystrophies, like obesity, with affections of the thyroid.

It is still a question how far in the direction of what is ordinarily called "health" we ought to extend our conception of the thyroidal cachexia; whether, for example, it is probable that some of the changes ordinarily attributed to old age—and, on the other hand, the various slight defects in tendencies of growth, in children, or of nutritive weaknesses in adults, such as those showing themselves in the parts of mothers in impaired reproductive powers, or failure to provide properly for the growth of the fœtus—are due to lack of thyroid secretion.

As regards the failure of nutrition in *old age*, Ewald expresses the opinion that it is due, not to atrophy of the thyroid but to impairment of the intestinal absorption; but we have no sufficient data for deciding as to the relationship of *obesity*, *tetany*, *scleroderma* and *rickets* to thyroid atrophy, except the inadequate argument from the success or failure of treatment.

This subject of *obesity* in its relation to thyroid treatment was discussed at the Congress of German physicians at Weisbaden, last year, and Spitzer there pointed out that a sharp distinction should be made between the obesity due to food and mode of life, and that due to lack of metabolic activity on the part of the tissues. Theoretically, it would only be in the latter form that thyroid preparations, which are a powerful stimulant to proteid metabolism, ought to be of special service. Ewald, however, in his recent monograph on the thyroid diseases,* says that in practice he has not found this distinction tenable.

If this argument from the effects of treatment is not considered decisive as against the thyroidal origin of a given disease, then the very interesting cases reported by Dercum and Henry† ought to be recalled in this connection. Here a peculiar form of subcutaneous dystrophy with accumulation of fat was present, and in two instances the thyroid was demonstrated to be calcareous. Ewald

* Nothnagel's Specielle Path. u. Therapie, l. c.

† American Jour. of Med. Sciences, Nov. 1892.

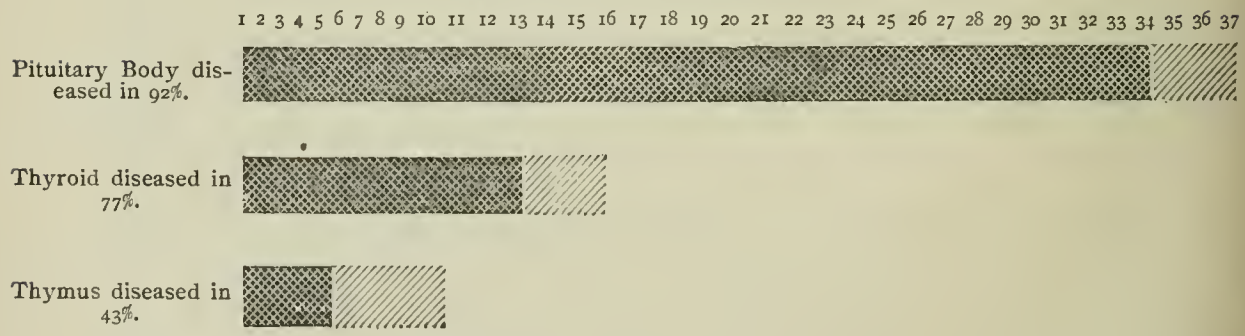
reports that he has seen another case of similar sort to these. I would again suggest that the relationship of obesity, etc., to the thyroidal cachexia may be similar to that of progressive muscular dystrophy to infantilism, and, in a similar sense, the various forms of idiocy which, as Bourneville says, are conjoined with the thyroidal cachexia without being of thyroidal origin, may perhaps be in a sense related to it.

It is a noteworthy fact that the true cretin is not helped by treatment with thyroid preparations to anything like the extent that the so-called sporadic cretin or myxœdematous child is. This shows either that the cause of his disease lies further back than the loss of his thyroid, both the goître and the cretinism resulting perhaps from the same influence, or else that the condition is a complex one and only partly of thyroid origin; but it does not show that thyroid disease has or had nothing to do with his symptoms, any more than the failure of an attempt to cure tabes by mercury shows that disease is not of syphilitic origin.

The only clinical data which have as yet thrown much light upon the functions of the *pituitary body* are those which have been gathered in the study of acromegaly.

It is beyond a question, as a glance at the accompanying charts 1 and 2 will show,* that a close connection exists between disease of the pituitary body and the symptoms of this affection, and a moder-

Autopsies in Acromegaly.



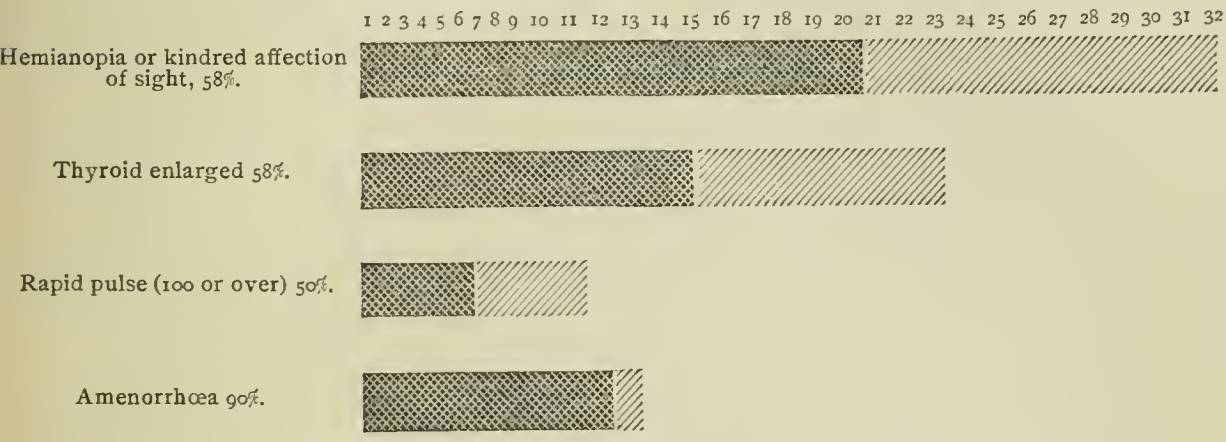
The black portion represents the number of cases in which lesion was found; the lighter-shaded portion represents the number of cases in which the organ is stated to have been normal. In the other cases no statement was made as to the organs. The line at the top gives the number of cases. The percentages are given in round numbers.

ately close connection between acromegaly and thyroid disease, but, as to the nature of these associations, neither physiological experi-

* Based on reports collected for me with great care by Dr. Franklin W. White.

ment nor pathological research has as yet enlightened us. The character of the pituitary disease varies greatly, but the fact that the organ is commonly enlarged is shown by the frequency with which hemianopia, presumably from compression of the optic nerves, is present during life.

Significant Signs and Symptoms in 35 Recent Cases.


1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25 26 27 28 29 30 31 32
Hemianopia or kindred affection of sight, 58%.
Thyroid enlarged 58%.
Rapid pulse (100 or over) 50%.
Amenorrhœa 90%.

What is the relationship of acromegaly to gigantism? May this also be of similar character with that between eunuchism and infantilism? Marie,* the author of our first carefully drawn descriptions of these affections, thinks there is nothing in common between them, and that the frequency with which the two conditions are associated is due solely to the fact that when the acromegalic tendency occurs during the period of growth, it causes increase in height, suggesting gigantism; whereas, if it occurs in adult life, the hypertropic tendency is expended on the extremities of the long bones. Sternberg† believes that gigantism, although not a disease, and not due to disease of the pituitary body, is a condition which, like infantilism, readily associates itself with all sorts of dystrophies—a view identical with that expressed by Meige with regard to infantilism—and that chief among these dystrophies is acromegaly, which *is* a disease.

It seems to me, however, that when it comes to drawing sharp distinctions between "disease," and "abnormality such as readily associates itself with disease," the task is a hard one, and that the evidence brought forward by Dana,‡ Brissaud,§ Massalongo,

* Bull. soc. med. des hôpitaux de Paris, 1896, 3d Ser., Vol. xii, 443, 413.

† Zeitschrift für Klin. Med., 1895, Vol. xxvii, p. 86.

‡ Journal of Nervous and Mental Diseases, 1883.

§ Bull. soc. med. des hôp. de Paris, 1896, xii, 443, and elsewhere.

Walker,* Hutchinson,† Schwoner,‡ and by Sternberg himself, showing the frequency with which acromegaly and gigantism, or unusual development in point of size, are associated, and associated even (Schwoner) in an hereditary sense, is too impressive to be made light of. Sternberg says that about 20% of cases of acromegaly show giant growth; and that about 40% of giants appear to have acromegaly. The only case of acromegaly which I have seen affected a woman decidedly above the usual size.

I have not thought it necessary, for the purpose of this discussion, to enter at length on the question of the disease of the pituitary body, or the thyroid, in relation to acromegaly, and will say, in brief, that thirty-seven post-mortems have been reported in cases of acromegaly, and that with three exceptions disease of the pituitary body was present in all. In the large majority of cases where the thyroid has been mentioned it was found diseased (10 out of 13). The affection is at any rate due to a deep-seated disorder of nutrition in which these organs are immediately concerned.

If one casts a glance over this whole range of diseases that we have been hurriedly considering—eunuchism, infantilism, acromegaly, cretinism, infantile and adult myxœdema, and considers what sort of departures from normal states they represent, the suspicion becomes grounded that they can be brought into some sort of harmony with each other. These affections are all substantially toxic in origin, and all except perhaps gigantism are in great part due to the loss or disease of an important organ—the testicle, the pituitary body, the thyroid and kindred glands—or else join hands with the loss of the special organ as being both expressions of a developmental defect lying further back.

But the point is that, in either case, the symptoms and anatomical changes are not to be looked upon as fortuitous combinations of morbid signs whose only bond is that they are all due equally to a common poison; nor is the term poison an adequate one to describe the agency that is at work.

What we see is—more or less vaguely to be sure— that under the conditions stated, a new "set," as it were, is given to the developmental forces of the individual. The eunuch and the ox, the infantile or feminine man, the giant, the cretin, are not simply stunted and poisoned specimens of life; they represent attempts at reorganization on new lines. In myxœdema and kindred diseases this

* Jour. of Am. Med. Assoc., 1897, Vol. xxviii, p. 169.

† Med. News, 1897, Jan. 16, p. 86.

‡ Zeitschrift für Klin. Med. 1897, Vol. 32, p. 202. [Supplement.]

principle is less evidently at work, and the signs of the action of a poison seem more evident; but it may, nevertheless, be profitable to study them on these same lines.

The poison does its specific work, but the poison is really a modification of some substance standing in a relation of close co-ordination with physiological processes.

The next subject for consideration is that of the *etiology* of *Graves' disease*, which represents a thyroid affection of another sort.

What is the part played by the thyroid secretion in producing Graves' disease? This is still a burning question among neurologists, and one of both theoretical and practical interest. It would be desirable to approach the solution by trying to answer the following questions:

1. How shall we define Graves' disease, and is there but one affection that deserves this name, or are there various forms differing in symptomatology, etiology, and prognosis?

2. Is the Graves' complex due purely and simply to thyroid poisoning, so that liability to the disease means only liability to disease of the thyroid; or is there a susceptibility due to peculiarity of the nervous system, and are there cases where this is the controlling factor? In other words, can Graves' disease occur without a thyroid, and if not, can an analogous disorder exist on these terms, and what are its peculiarities?

3. Assuming that the thyroid secretion is the cause of the symptoms as we see them, can we, nevertheless, show that the thyroid disease is often secondary to events taking place in the nervous system?

4. Still assuming that the thyroid secretion excites nervous symptoms, does it do so in proportion to its amount; or is it possible, on the other hand, or even probable, that there is no direct proportion between the amount of excess of the secretion and the severity of the symptoms, so that a small gland is as likely to be associated with marked symptoms as a large gland?

5. To what extent is it possible to localize the lesions of the nervous system associated with Graves' disease?

6. What is the value of the arguments as to the nature of the disease drawn from the effects of surgical or other therapeutical measures?

7. Is there any good reason to suppose that there is a special thyroid poison which is necessary for the production of Graves' disease, and which does not exist in the normal gland?

I shall try to answer some of these questions, though not in a systematic way, and shall offer, as in my opinion the most profitable point of view from which to study the subject, the suggestion that Graves' disease is the distorted representation of a physiological or quasi-physiological mechanism, and that just as emotional states and nervous states in general are intimately associated with more or less specific changes in general metabolism, so a similar association exists here, but that it has become dislocated and perverted in such a way that toxic symptoms result.

As regards the purely clinical evidence as to the nature of Graves' disease, every one must appreciate the force of the arguments which refer the symptoms to a poisoning with a thyroid secretion, and which makes it appear that the thyroid disease is a primary lesion. This view is held by some of the best observers in every country, among whom is Horsley, whose name has been identified with the best work on the thyroid, for so many years.

The general nature of these arguments is familiar to every one. The thyroid is almost always enlarged in Graves' disease, and where it has not been found enlarged during life, histological changes have been discovered post-mortem.

These changes are almost always what is called hypertrophic; that is, they are such as to secure a larger secreting surface, and although the secretion is usually deficient in colloid, it is nevertheless functionally efficient, as is shown by the fact that myxœdema does not occur, and that preparations made from the gland of a patient with Graves' disease have much the effect as those made from normal sheep's gland (Hutchison).*

The symptoms of Graves' disease are almost certainly due, in part, to some poison, and experiments with thyroid preparations, both upon men and animals, indicate that the thyroid secretion is capable of producing analogous symptoms to those found in Graves' disease. It is also pointed out that the symptoms in Graves' disease are, in some respects, the converse of those seen in myxœdema; in other respects, similar to them.

In spite of these considerations, it cannot be said that the thyroidal theory is in all respects satisfactory; and, hitherto, it has failed to command anything like universal approbation.

The symptom-complex of Graves' disease is richer and at the same time far more varied than that producible by thyroid preparations. The reasons for assuming an excess of secretion are by no

* Brit. Med. Jour., 1896. Vol. ii.

means always sufficient, the more so that a partial atrophy of the gland, sufficient to excite myxœdematous symptoms, is no necessary bar to the persistence of some of the symptoms of the Graves' complex. To meet these difficulties, it has been suggested that the thyroid secretion is not necessarily increased in quantity, but may be altered in character. This is possible, but of the fact of such alterations we have no knowledge, and the experiments of Hutchison,* who made preparations from the excised thyroid from a Graves' disease patient, and studied their effects on both men and animals, indicated no difference between secretion and that of an ordinary gland. Moreover, if we assume that the secretion has specific functions in Graves' disease, then we have no right to apply to it the arguments drawn from the studies of the normal secretions. Various other criticisms of the thyroidal theory and also various other arguments in its favor could be adduced, but I will refer only to those based upon the effects of surgical treatment by thyroidectomy and on the difference in apparent etiology and type between different groups of cases.

Can we infer from the fact that a patient improves more or less after the partial removal of a parenchymatous goître in Graves' disease—perhaps only a long time after—that the goître was itself the cause of the symptoms?

I believe that this method of reasoning is mistaken in theory and inconclusive in practice. The question is an interesting one, but I will dwell upon it no longer than to recall that most of us do not believe that because the removal of this or that peripheral irritation makes it easier for a patient to deal with some neurotic tendency, therefore the cause of the neurosis has been discovered. A failure to appreciate this has led to many an erroneous conclusion, as, for example, in regard to the relation between eye-strain and epilepsy or migrane.

If the argument from the success of thyroidectomy is to be held up as conclusive, then the door is open to many new etiological theories based on similar grounds.

For the vicious circle, of which the gland forms one link and the nervous erythism another, has been successfully broken into by many agencies, electricity, diet and intestinal antiseptics, thymus, and last but not least, by treatment of the nature of hypnotic suggestion.

In talking of the etiology of Graves' disease, have we a right to

* L. c.

assume that the cases to which that name is usually applied are always of one or the same sort? From the clinical standpoint wide differences are to be seen in respect to etiology, mode of onset, symptomatology, and prognosis.

Who has not seen cases where a person, apparently healthy, has been plunged almost at once, in consequence of some terrifying emotion, into a state closely resembling Graves' disease, and leading directly to that disease in its most profound form?

And, on the other hand, who has not seen similar symptoms, appearing little by little, in a patient who has had an indolent goître without symptoms, perhaps for years; or both conditions coming on gradually in connection with chlorosis, or in girls of feeble health?

It is the first class of cases that makes it seem almost imperative to regard Graves' disease as a fright-neurosis, while for the cases of the second class, the nervous symptoms are often regarded as secondary (Buschan,* Marie,† and others), and it is pointed out that the eventual nervous symptoms in cases of this sort are rarely so severe or so numerous as in those of the former group.

It must not be forgotten, however, that intermediate cases exist between these two extremes, and that many cases are to be seen of either class which when fully developed are indistinguishable from those of the other.

An interesting example of the intermediate forms is afforded by the history of a family of a mother and nine children, from Aveyron, reported by Sottas.‡

The mother had a goître associated with dyspnœa and palpitation; a daughter had a goître without nervous symptoms; a second daughter had dyspnœa without goître; a third daughter had a typical, serious Graves' disease induced by severe emotion during which the heart action was powerfully affected; a fourth sister had Graves' disease but in a less pronounced form and also of emotional origin. Four sons and one daughter remained free.

The acute cases are not always of emotional or nervous origin, as is shown by an interesting instance reported by Van Noorden in his recent monograph on chlorosis.§ In this case the typical Graves' complex sprang into existence, rose to a high point, and

* Basedowsche Krankheit, Leipzig u. Wien. 1894, and elsewhere.

† See Rev. Neurologique, Feb. 15, 1897.

‡ France méd., 14 août., 1896. (Analyzed by Feindel, Revue Neurol., Feb. 15, 1897.)

§ Nothnagel's Specielle Pathologie und Therapie, Bd. viii, 11.

again disappeared, in the course of a single week, while the patient, a chlorotic young woman, was under observation in the hospital. The thyroid swelled and again shrank and finally disappeared, as the symptoms advanced and receded. Yet no fright or other obvious nervous excitement could be discovered as having preceded this outbreak.

It should be said that Van Noorden does not believe that chlorosis is the cause of Graves' disease or that the two affections are especially apt to be associated.

The cases arising under the influence of pregnancy and (perhaps) from intestinal poisons, or without apparent cause, are other sorts which do not fit exactly in either of the first mentioned categories.

Considering these discrepancies, and remembering that a vastly greater number could be cited, it seems to me idle to expect that we can frame a really satisfactory and comprehensive theory of Graves' disease until we learn to penetrate far deeper than is now in our power into the mysteries which shroud the activity of the nervous system, and its relationship to the thyroid gland and to processes of general metabolism, in health.

Every exclusive theory of the present moment is bound to be inadequate, but the consideration of each is likely to be profitable, if it secures us a clearer sight into the physiological and pathological principles that are involved.

One such principle is that the neuroses in general, among which Graves' disease is, to a certain extent at least, to be classed, owe their characteristics to the fact that they represent distorted and caricatured images of physiological arrangements, separated to a greater or less degree from their natural associations. The mechanism of which they are a caricature was designed to play a subordinate or coördinated part in furthering the ends of the economy as a whole, but as seen in disease it is segmented off and enters into independent activity and becomes enlarged and disfigured by forming new associations. By studying the peculiarities of such a neurosis, we can often get a side light upon the normal conditions.

The symptoms of Graves' disease shade off, if one studies a large number of cases, into the phenomena of health. The tremor, the rapid and excitable pulse, the flushed skin, the restlessness of mind, are seen almost habitually in many persons who are called simply nervous, and these symptoms and more, including the staring gaze, may come on suddenly, even in a presumably healthy person, under the influence of strong emotion, which may be called either a disease or a quasi-physiological state. In fact, the Graves' disease

complex is but one of the wide range of results to which emotional disorders may lead, each of which must have its definite pathology. Anything which can be ascertained with regard to the physiological and chemical pathology of emotion is likely to throw light on the nature of Graves' disease, and vice versa. From this standpoint, the toxine theory of Graves' disease becomes of special interest. If it is true, as Moebius—the able defender and essentially the author of the thyroid theory—suggests, that a sudden fright does not cause Graves' disease except where the thyroid was previously in an unstable condition, then it is equally likely that physical signs of fright, even in those cases where these signs subside more or less quickly, arise more easily when the blood contains certain constituents which render the nervous system more sensitive in this or that special way. Chemical theories of physiological processes seem less foreign to-day than they would have seemed a few years ago, and there is nothing especially unreasonable in the view that emotional states of more or less definite sort are foreshadowed in the metabolism of the individuals who are liable to them, just as habitual thoughts occur most readily the more readily they find the appropriate expression awaiting them.

If it is really the thyroid secretion (or some other product of disordered metabolism) that excites the symptoms of Graves' disease, then it may be that the presence of this secretion in the blood helps to insure the mobility of the nervous system in certain respects in health.

If the thyroid secretion has nothing to do, etiologically, with fright, then there is the more reason to think that the emotional form of Graves' disease is not of thyroid origin, and we may rest content with our old physiological theories as to the cause of the physiological element in fright.

I venture to suggest, at any rate, that if the thyroid secretion is the usual excitant of the Graves' complex, it acts like a match applied to a combustible, by giving the final impulse necessary to the outbreak of the disease, rather than by exciting symptoms proportionate to its own amount. This seems to be borne out by the fact that the severity of the symptoms is by no means in the same ratio with the size of the gland, the most violent nervous symptoms sometimes being associated with a very small gland, perhaps one which cannot even be felt, while the reverse is equally true. Again, the additional administration of the thyroid preparations does not by any means necessarily increase the symptoms, as my own expe-

rience and that of others has abundantly shown. The degree and nature of the susceptibility seems to be the controlling factor.

If my view is correct, that, under the appropriate conditions as regards susceptibility, a small amount of the thyroid secretion may suffice to precipitate the disease, we can easily understand why it should occasionally happen that myxœdematous symptoms are associated with those of Graves' disease.

In the great majority of the reported cases of this sort, the myxœdematous symptoms have supervened on those of Graves' disease, and it might be said that the latter had simply lasted over from acquired habit. But occasionally the sequence is reversed, and an interesting case of this sort has been communicated to me by Dr. Osler.

I will only repeat, in conclusion, that the importance of the analogy between Graves' disease and health is urged, not as an exclusive theory, but as one profitable mode of regarding the subject.

INTERNAL SECRETIONS CONSIDERED IN THEIR PHYSIOLOGICAL, PATHOLOGICAL AND CLINICAL ASPECTS.

The Therapeutics of the Internal Secretions.

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The various theories which have been deduced from experimental, pathological, and clinical observations of the functions of the ductless glands, together with a review of the results of therapeusis in their various diseases, based upon such theories, will be presented in this paper.

Although it has long been surmised that the secretions of the ductless glands were of vital importance to the bodily economy, it is only lately that they have been shown to rival in their *rôle* the part played in metabolism by the glands provided with ducts, such as the liver and pancreas.

The Thyroid Gland. Experimental, pathological, and clinical investigations have demonstrated the vital importance to the economy of the physiological function of the thyroid gland. Defective development, pathological changes, destructive or otherwise, and experimental removal, induce a train of well-known symptoms which necessitate the acceptance of one of two theories as to the nature of its function:

1. That its office is chiefly, if not wholly, a secretory one; that it furnishes some material which enters the blood, probably through the lymphatics, and which is essential for the chemistry of metabolism and for the proper nutrition of the various tissues.

2. That its function is to neutralize or destroy certain poisons which result from tissue-changes, and which, by their tendency to accumulate in the blood, induce autointoxication.

The arguments, and they are many, which may be advanced in favor of either one of these theories, will be more properly considered in the papers devoted to the physiological and pathological aspects of the subject. Experimental and clinical observations have demonstrated that the *specific* function of the gland, whether it be to aid metabolism or to develop an antitoxin, can be replaced by a suitable dosage of extracts or preparations of the normal gland administered subcutaneously or by the digestive tract. If the

specific purpose of the gland is antitoxic, it is thus evident that this function can be effectively exercised in the blood-current or tissues, even if normally it is partly or chiefly effected within the gland-substance.

In diseases, therefore, which have been shown to be due to a loss of function of the thyroid gland, myxœdema, cretinism, both sporadic and endemic, and operative myxœdema (cachexia strumipriva), the indication for treatment is direct, and the results are among the most brilliant examples of the value of a therapeusis which is based upon experimental pathology.

The number of cases of myxœdema treated with the thyroid preparations is already very great, and experience justifies the formulation of many practical rules in this method of therapeusis. The most important of these rules were to be inferred from the pathology of the disease. Although the myxœdematous symptoms are speedily removed by the treatment, a discontinuance of the treatment is certainly followed by a return of the myxœdema at varying intervals, showing that the treatment does not cause the gland to resume its function, but exercises its influence by introducing into the economy something which it is presumably the function of the gland to supply. It has been shown conclusively, first, that complete recovery can be effected even after the disease has existed for as long a period as fourteen years and in the case of patients bedridden and presenting the gravest symptoms; and, secondly, that the maintenance of health can only be secured by continuous treatment during the lifetime of the patient. The requisite dosage after the removal of the myxœdematous condition has been found to vary, and depends upon the degree of loss of glandular function. Equally good results are obtained from a single daily dose or a larger dose given at longer intervals. It has been found that this interval rarely can exceed a week.

The complete restoration of physical strength, aside from the general well-being of the patient, is well illustrated in a case of Murray's,[1] a male, who from being practically disabled, at the end of two years after the beginning of treatment was able to make the ascent of a mountain 3000 feet high, including a walk of ten miles, without any undue fatigue.

It may be of interest to refer to the subsequent history of a woman, forty-three years of age, under my personal care, who was among the first to be treated by thyroid preparations in this country (1892). The disease had existed for twelve years; she had been

bed-ridden for a year; she had lost her hearing, was hairless, and suffered from marked mental hebetude and grave physical prostration. After the marvelous improvement usually effected in the first few weeks of treatment she continued to improve, and for the past two years she has admirably filled a responsible librarian's position in addition to performing easily all the duties of the head of a household. Her hearing is perfect; she has a new growth of hair of the finest fibre, reaching to her waist, and the brilliant coloring and texture of skin rarely seen except in youth. She maintains her present condition of health by taking the equivalent of five grains of the fresh sheep's thyroid twice weekly.

Cretinism, sporadic and endemic. Continued experience during the few years which have elapsed since the treatment of cretinism with thyroid preparations was first instituted has confirmed the hopes which were originally entertained of its efficacy. It has been shown conclusively, first, that in sporadic cretinism the myxœdematous symptoms can speedily be removed, thereby effecting a marvelous improvement in the frightful deformities incident to the disease; secondly, that the treatment is capable of developing the natural tendencies of the growth of the skeleton which were in abeyance, and that this latent capacity is in apparent inverse ratio to the age of the patient; thirdly, that a striking improvement in the mental condition is effected, although occurring more slowly and in a similar inverse ratio to the age of the patient, as observed in the skeletal growth. The rate and degree of the growth of the skeleton at different ages are strikingly illustrated in the cases of cretinism reported by Thomson[2] at the last meeting of the British Medical Association. In the case of a child, five years of age, who was seven inches below the normal height at the beginning of treatment, the growth was five and three-quarters inches in the first year of the treatment, four and one-quarter inches in the second year, and two and one-half inches in the third year. In a girl of eighteen years the growth was four and three-quarters, two and three-eighths, and one and three-eighths inches in the first, second, and third years respectively. And, finally, in two adult cretins, thirty-six and thirty-nine years of age, the growth in one was three-quarters of an inch and five-eighths of an inch in the first and second years, and none in the third; in the other, one and seven-eighths and three-quarters of an inch represented the growth in the first and second years, and there was no further growth in the third. These results are very similar to those reported by many other observers.

The radiograph has been utilized by Hertoghe for purposes of prognosis in cases of this kind. The completeness or incompleteness of ossification, demonstrable in this way, indicates the possibility of further skeletal growth.[3]

An interesting point in the skeletal growth is that, as the child approaches the height normal at a definite age, continuous growth apparently is only at the usual rate. In the very rapid growth of the bones a tendency to softening, resembling that which occurs in rickets, has been noted by several observers, and has been ascribed to the use of doses of the thyroid extracts which were probably too large. It is, perhaps, too soon to speak positively of the degree of mental improvement attainable; but already cases of cretinism in children have been reported where the intelligence, after three years of treatment, has compared favorably with that of normal children of a similar age.

In view of the facts related it is not unjustifiable to conclude that the treatment of cretinism with the thyroid preparations, if initiated early in the disease and systematically continued, holds out every promise of the child's development into a healthy adult.

The therapeutic value of thyroid preparations in cretinism has suggested their use in cases of idiocy more or less resembling in bodily and mental defects the cretinous condition.

Bourneville has shown that the weight of the thyroid gland varies very considerably in different cases of idiocy.

Telford Smith[4] has tried the treatment in idiots belonging to the Mongol type, who most closely resemble the cretin. His experience has been that a physical and mental improvement occurs, and that it is inversely to the age of the patient; that the improvement is neither so rapid nor so marked as in the cretin. There is some improvement in the condition of the skin; it desquamates, but does not become normally smooth; chronic marginal blepharitis improves and in some cases is cured. Growth improves as well as the mental condition.

Goître. Turning from a consideration of the thyroid treatment in pathological conditions necessarily involving a loss of function of the thyroid gland to other morbid conditions in which its functions may be variously affected, goître first attracts our attention.

The benefit derived from the use of the thyroid preparations in cases of goître in which the absence of constitutional symptoms indicates that the function of the thyroid gland is still largely preserved, has not been satisfactorily explained. The benefit consists

in a retrogression of the goître through atrophy of the hyperplastic and adenomatous tissues.

The maximum improvement is obtained in goître of the simple hyperplastic form, although adenomatous nodules in many instances shrink in a striking manner. Large collections of colloid and cysts are apparently unaffected by the treatment. The diminution in the size of colloid goîtres Kocher attributes to a shrinking of the parenchymatous tissue in which the colloid is imbedded. Although marked diminution in size in the varieties of goître which have been mentioned, and a corresponding improvement in the patient's general condition occur, complete disappearance, at the tumor has rarely been noted. The reports of various observers of the permanent improvement or cure are not sufficiently full to justify positive statements on these points at the present date. Recurrence of the tumor after partial or complete disappearance, at varying intervals after the discontinuance of the treatment, certainly occurs in many instances, and suggests the possibility that continued use of the thyroid preparations in a modified way for indefinite periods may be found necessary.

Bruns has reported 60 cases,[5] non-malignant and non-cystic in character, treated by this method; 14 were cured, 29 were improved, and 17 were not benefited by the treatment.

In 21 cases reported by Knœpfelmacher,[6] in 11, the patients varying from two to seventeen years of age, the retrogression of the goître was marked, although in none was it completely removed; of these, 9 cases were of the hyperplastic type. In 5 other cases of colloid goître a perceptible diminution in the size of the tumor was effected. In the remaining 5 cases no improvement was observed.

Angerer[7] has treated seventy-eight cases with thyroid preparations, and claims that in all the cases in which the treatment was tolerated and continued for a period of several weeks diminution in the size of the goître was attained. The most striking results were noticed in the soft goître of the simple hyperplastic form, and especially in those occurring about the age of puberty. In cystic goîtres, through the atrophy of the hyperplastic tissues, the cysts became more superficial, and their enucleation was thereby rendered more simple.

In eighty-three cases of Stabel's, improvement was obtained in 92 per cent. In only two was there unquestionably permanent recovery. Stabel[8] states that after the administration of thyroid substance was discontinued, the tumor, in cases in which it had

decreased, again began to increase in size at varying intervals of four to six weeks.

In explanation of the action of thyroid gland preparations in goître, Bruns, Ewald, and others have suggested the hypothesis of a primary toxæmia of unknown origin, which evokes an increased functional activity of the gland, accompanied by hypertrophy. If the demand for thyroid products is supplied artificially, the gland retrogrades and atrophy results.*

Exophthalmic Goître. *A priori*, benefit would not be expected from the thyroid preparations in exophthalmic goître, as increased functional activity of the thyroid gland probably occurs in this disease, and the preponderance of evidence indicates that their use is commonly attended with an aggravation of the symptoms.

In certain cases, however, the employment of thyroid extracts is unattended with any appreciable effect. The natural fluctuations of the disease, improvement alternating with recrudescences, suggest that the exceptional reports of *improvement* under this treatment have been based upon insufficient grounds.

Finally, the thyroid treatment has been employed in various pathological conditions in which a perversion of the function of the thyroid gland has yet to be proved.

Without such perversion it is probable, from the power of the active principle to quicken metabolism processes, that the treatment would be of value.

Insanity. The use of thyroid preparations in the treatment of various forms of insanity was originally based upon its undoubted power to increase ultimate cell-metabolism.

A relatively large number of cases treated by this method have been published. Bruce[9] has reported 60 cases, 25 males whose ages ranged from twenty to fifty-five years, and 35 females whose ages ranged from twenty to fifty years. Of the males 7 recovered under treatment, and there were 17 recoveries among the females. Thirteen of these latter were either puerperal, lactational, or climacteric cases.

Bruce believes that the action of thyroid in insanity is a complex one.

1. That the feverish condition induced by it is of benefit to the patient.

2. That it acts as a direct cerebral stimulant.

* Bauman's isolation of an iodine-bearing compound (iodothyrine) from the thyroid gland secretion suggests an explanation of the value of iodine in the internal treatment of goître.

3. That it supplies some material necessary to the economy which the gland is supplying in sufficient quantity.

Babcock has published twenty-two cases treated in the St. Lawrence State Hospital for the Insane.[10] In four cases there was recovery; in eleven, improvement. The four recoveries were in patients suffering from recurrent mania and melancholia. Improvement was obtained in cases of acute mania and acute melancholia, in two cases of acute delirium, in a case of chronic mania, and in one of chronic melancholia. Relapses occurred in four cases. In one of these (chronic melancholia) relapses followed two successive treatments.

Allen Starr's[11] extensive experience has led him to place the highest value upon the treatment* in a form of mental disturbance occurring at the climacteric. He describes it as a mental depression with anxiety and morbid fears, but without delusions or insomnia. Starr is inclined to believe that a functional disturbance of the thyroid and ovaries is associated in these cases.

These results correspond closely with those obtained by various other observers and indicate a decided advance in the therapeusis of certain forms of insanity. The favorable or unfavorable response to the treatment is even accepted by several distinguished alienists as affording a basis for prognosis in the large class of cases occupying "the borderland" between curable and incurable states.

Obesity. The literature of the thyroid treatment of obesity is already very voluminous. The number of published cases treated by this method during the past four years is large, and the results in general have been favorable.

The researches of Treupel, Grawitz, Roos,[12] and Hennig, among others, have shown that under the influence of the active principle there is a decided increase in the excretion of nitrogen as compared with the amount received in the diet.

In the discussion in the Fourteenth Congress for Internal Medicine, Ewald stated that the thyroid preparations influenced metabolism *in toto*, without a selective action on the fats, and hence that there was an albuminoid waste which should be compensated for by an appropriate diet. In certain cases he had found the treatment to be without effect, an experience which harmonizes with that of other observers, and that its failure was observed not only in the

* Clouston says "that large doses of thyroid are of marked benefit in cases which threaten to become chronic, and that no case should be allowed to become incurable without a trial of this method of treatment."

class of patients which accumulated fat in spite of a careful dietary, but also where the obesity is the result of excessive indulgence. In such cases the fatty deposits lie beyond the limit of the control of the oxidation processes.

In patients who react to treatment the loss of weight varies from 1 to 5 kilogrammes (2 to 11 pounds) a week, without restriction of diet, but after a time a limit is reached beyond which further reduction is not obtained. The loss of weight is more rapid during the first days of treatment than later; subsequently it varies in amount from week to week, without explainable reason, the conditions of life remaining the same. The loss is usually unattended with any disturbance of health. As a rule, the discontinuance of treatment is quickly followed by an increase of weight, which shortly reaches its former level. Only exceptionally is the improvement maintained for any considerable period, although careful dieting and exercise prolong its duration.

Cutaneous Diseases. The expectations originally entertained of the value of thyroid treatment in diseases of the skin have not been fulfilled. Only in psoriasis has some small measure of success been obtained. Even in this disease the effects are uncertain; it is impossible to differentiate the type of the affection in which benefit may be expected, and in many cases an aggravation of the lesions occurs.

Phthisis. The suggestion of the possible value of thyroid preparations in phthisis rests on the slender basis of their temporary effects in some cases of lupus, upon the assumed antagonism of goître and tuberculosis, and finally upon the atrophy of the thyroid gland in chronic, wasting diseases. Morin[13] and Kraus claim favorable results from their use.

As early as 1893 the treatment was instituted in my hospital wards in carefully selected cases of pulmonary tuberculosis, and the conclusions reached were that it was absolutely without effect either upon the lesions or the general condition of the patient.

The use of thyroid preparations has been further extended, and claims of their therapeutic value in various other morbid conditions have been made.

Further careful investigations and corroboration are demanded before they can be finally accepted.

Attempts have been made by various investigators to isolate the specific principles of the thyroid. Exclusive of Fränkel's discovery of a substance of active properties, but which does not prevent the

occurrence of the chronic cachexia, Baumann has isolated an iodine-bearing compound of albumin and globulin, which he has named "Iodothyrine."[14] He believes it to present the total specific activity of the glandular extract, which he makes dependent upon the amount of iodine it contains.

R. Hutchinson[15] has within the last few months published the results of his investigations into the active principles of the thyroid, which in the main corroborate those of Baumann. He finds that the thyroid contains two proteids, viz., a nucleo-albumin and a colloid matter; the former is small, the latter large in amount. The colloid contains a small amount of phosphorus and a considerable proportion of iodine. On gastric digestion it splits up into a non-proteid and a proteid portion, both of which contain iodine, but chiefly the non-proteid portion.

The colloid matter is the only active constituent of the gland in a specific sense. Both the non-proteid and the proteid portions of the colloid are active, but the former (apparently identical with Baumann's iodothyrine) is much more so than the latter.

The Adrenals. With the exception of Tizzoni's[16] notable experimental investigations, from which he concludes that the adrenals are functionless and derive their importance from their anatomical relation to the sympathetic, all modern work strongly indicates that they are functionally active glands.

The theories advanced in regard to the nature of their function are:

1. That their office is to neutralize or destroy certain toxins and effete blood-pigments which are constantly accumulating in the blood; that their function is excretory.

2. That their function is a secretory one; that they elaborate some substance which enters the circulation and which is necessary to the economy.

Excretory theory. The excretory theory is based largely upon the apparent toxicity of the blood of animals deprived of their adrenals[17]; upon the respective effects of injections, into the peritoneal cavities of rabbits, of solutions of nicotine which had been kept in contact for varying periods with fresh adrenal tissue, and solutions of nicotine of the same strength with or without contact with muscular or renal tissue (Charrin and Langlois[18]); upon the effects of atropine upon completely acapsulated animals (Abelous[19]); and finally upon the results obtained in guinea-pigs, normal and monacapsulated, by the injection of both sterilized and virulent cultures of the bacillus pyocyaneus (Langlois and Charrin[20]).

The conclusions of these observers are that the functions of the adrenals are to produce one or more substances designed to neutralize or destroy the toxins normally arising from muscular metabolism, and, perhaps, also certain poisons accidentally introduced from without, including those of bacterial origin.

Secretory theory. The secretory theory is based upon the physiological effects obtained experimentally by subcutaneous and intravenous injections of extracts of the adrenals.

Cybulski,[21] from an extended series of experiments, concludes that the adrenals furnish an indispensable secretion which diffuses continuously from the glandular parenchyma, more especially of the medullary substance, into the blood-current, its office being to maintain the activity of the vasomotor centres, the vagi and accelerator nerves, the respiratory centre, and with great probability, also, the centre which maintains muscular tonus.

He claims that the active principle can be extracted by alcohol or glycerin and a variety of other solvents, that it is not destroyed by boiling and will dialize. If the gland is boiled previous to extraction, it will not yield its active substance to water; or if it be dried at a temperature of 110° C., the alcoholic extract is inert and the watery very much weakened. When introduced into the veins of an animal it causes a marked but very brief increase in blood-pressure and a slowing and increase in force of the heart-action, with diminished respiratory effort. This effect is never obtained from similar preparations from the brain, spinal ganglia, lymph-glands, liver, spleen, kidney, testicle, or thyroid of the calf and ox.

By an independent series of investigations Schæfer and Oliver[22] have arrived at essentially the same results. Aside from some disagreement in a few particulars relating to the method of extraction and chemical peculiarities of the active agent, they differ from Cybulski chiefly in holding that the action is exercised directly upon the muscles, and not through the intervention of the nervous system. They reject the theory that the brief effect and rapid disappearance are due to oxidation, and suggest that the substance may be stored up in the skeletal muscles, and lay particular stress upon the exceedingly minute dosage which suffices to produce the vascular phenomena which they found so prominent.

They agree with Cybulski in localizing the active principle to the medullary portion of the gland.

They conclude from their investigations that the suprarenal

capsules are secreting glands which elaborate a material producing striking physiological effects upon the muscular tissue generally, and especially upon the heart and arteries, and that, therefore, one of the main functions, if not the *main* function, is to produce a material which is added in some way or another to the blood, the effect of which is to assist, by its direct action upon the various kinds of muscular tissue, in maintaining that amount of tonic contraction which appears to be essential to the physiological activity of the tissue.

Some very recent work indicates the presence in the adrenals of more than one active principle, and two theories attract our attention:

Mühlmann[32] believes that he has demonstrated the presence of a combination of pyrocatechin in the medullary substance. According to his hypothesis, it is one of the functions of the suprarenal capsules to convert the protocatechuic acid derived from the vegetable elements of diet into pyrocatechin. The latter substance in small doses elevates blood-pressure, while in larger doses it is toxic. The herbivora are less sensitive to its influence, probably as an effect of habituation. Its elimination or conversion into harmless products is believed to be accomplished through the intervention of some unknown activity of the ganglion-cells of the sympathetic. If the latter function fail or the pyrocatechin be produced in excess, toxic symptoms arise, accompanied by an abnormal pigmentation derived from the reaction between the tissues and this substance in the presence of alkalies. The author does not exclude the presence of other active principles and other functions of the gland, but considers his hypothesis to afford the best explanation of the toxic effect of adrenal extracts and the occurrence of pigmentation of adrenal origin.

Gourfein[24] and subsequently Dubois[25] have endeavored to isolate the various active principles obtainable from the suprarenal gland.

Without entering into the complex details of their chemical experiments, it is sufficient to state that Dubois has separated the active principles into two classes. The first is composed of several albumoses which may be precipitated with alcohol and redissolved in water. The substances so isolated have no well-marked toxic effect, but they and they alone seem to possess therapeutic importance, manifested by their influence in diminishing or even preventing the results of the injection of muscle-toxins. He regards these antitoxins as diastases or substances endowed with an inherent

dynamic activity which cannot be isolated from the protoplasmic bodies with which it is associated. The second class is composed of bodies which resemble in their constitution and reactions the alkaloids. They have a marked degree of toxic effect, and are identical in some of their reactions with the muscle-toxins. This leads the author to favor the theory that suprarenal bodies, like the liver, occlude the products of organic waste and modify them *in loco* by the action of special diastases.

Dubois concludes that the chief function of the suprarenal capsules is to destroy the toxins in circulation, especially those resulting from muscular waste and perhaps those furnished by the nervous tissue; that they do not seem to secrete any special substance destined to enter the general circulation, but that their cellular protoplasm possesses a special diastatic property, non-toxic, which seems to modify certain poisons, organic and bacterial, yet this action requires time, and proceeds little by little; that in normal conditions there are always alkaloids present, especially in the medullary zone, which possess an intense toxic action upon both striped and unstriped muscular fibre, and upon certain nervous elements not yet fully defined; that it is the retention of these excrementitious products which brings about serious symptoms; that their quantity may vary under the influence of numerous conditions; and that no positive therapeutic results can be obtained until we are able to separate definitely and completely the toxic and the antitoxic principles which coexist in the suprarenal capsules, as glycogen and its ferment coexist in the liver.

On the basis that the adrenals are functionally active, the employment of adrenal preparations has been advocated in pathological conditions necessarily attended with loss of function of these glands.

I have been able to collect forty-eight cases of Addison's disease treated with various adrenal preparations. They have been tabulated with brief notes of their salient points. Six patients are reported as cured or practically well, 22 improved, 18 unimproved, and in 2 instances an aggravation of the symptoms is stated to have occurred during treatment.

Among the six recoveries, in one instance the patient has remained well for four months; in a second case the treatment was continued for four and one-half months, the pigmentation disappeared, and the patient was able to return to work. He is still under observation one year and a half after the treatment was instituted, and is still well. In a third case the patient was practically

well at the date of the last report, twelve months after the beginning of treatment.

In the cases in which improvement was noted relapse and death occurred in one; in another the improvement was only temporary, death following; in a third case, the treatment was irregular, and the patient was relapsing at the date of the last report. In a fourth case improvement in the asthenia and pigmentation was observed until the end of the fourth week, when, the appetite failing, treatment was suspended, and death occurred two weeks later. In another patient there was marked improvement during regular treatment. During the subsequent months the treatment was irregularly pursued, and eight months later the patient was reported as failing rapidly. In Bramwell's case there was remarkable improvement for a year, the patient being able to resume his ordinary occupation, when death occurred. In still another case improvement had been maintained for twenty months at the date of last report. The patient had been able to return to work, but relapses occurred when the treatment was suspended. Finally, in one case there was improvement for three months, when the patient died quite suddenly on the discontinuance of the treatment.

In many of the cases related the association of adrenal disease with grave tuberculous lesions elsewhere in the body precluded the possibility of obtaining more than an amelioration of symptoms; nevertheless, the results secured justify the hope that perhaps with the isolation and differentiation of the several active principles, if several there be, of the glandular structures, an efficient therapeusis may be obtained for the simple atrophies and fibroid degenerations of the adrenals, which it has been demonstrated may be both localized and provocative of some of the phenomena of so-called Addison's disease.

The rise of blood-pressure produced by the active principle of the adrenals, through its action either directly or indirectly upon the muscular walls of the blood-vessels and the heart-muscle, has suggested the possible therapeutic value of the adrenal preparations in pathological conditions other than those necessarily attended with loss of function of the gland.

Where the vasomotor tone is lowered, as in asthenia and anæmia, their use would seem to be indicated, and Oliver[26] claims benefit has been noted. In cyclic albuminuria he also states that he has obtained good results from their employment. Oliver also suggests their probable value in heart-failure, as there seems to be some

resemblance between the physiological action of the active principle and that of digitalis. In a few cases of this kind adrenal extract has very recently been tried in my hospital wards, and with apparent benefit. The rapid rise in blood-pressure was distinctly shown by the sphygmograph, and was also appreciable to the finger. Further study is necessary to determine their true therapeutic value in the conditions mentioned.

Schaefer and Oliver's investigations indicate that the active principle is not unfavorably influenced by gastric digestion; hence that the various preparations properly may be administered by the mouth, and again, that comparatively large doses may be given to man with safety. A daily dosage equivalent to 45 grains of the fresh gland is recommended for therapeutic use. It can be given continuously for very long periods without injurious effect.

Thymus Gland. The determination of the true physiological position of the thymus gland in the human economy is especially difficult on account of the several histological phases in its natural history.

Closely related to the thyroid gland in its manner of origin, the structure of glandular epithelium of the first four months of intrauterine life gradually gives place to a lymphadenoid structure which reaches its maximum development at birth. This lymphadenoid thymus is normally present until the period of puberty, when it is gradually replaced by the lobulated fatty thymus, which persists indefinitely in man.

It would, therefore, seem that the existence of a secretory function is presumable only in the first months of intrauterine life. Whether the function of the lymphadenoid thymus differs from that of other lymphadenoid structures yet remains to be determined. The discovery by Baumann of minute amounts of an iodine-bearing compound in its tissues,[27] a substance not found in other organs, with the exception of the thyroid gland, is suggestive.

It is thus evident that the physiological basis for the therapeutic use of thymus gland is a slender one.

Clinically, the original employment was accidental, and explanations of its action at present must be regarded as largely speculative.

Owen's published case of exophthalmic goître,[28] in which benefit was observed from feeding with thymus gland which had been used by mistake for thyroid, introduced the thymus treatment of this disease.

I have collected 62 cases of exophthalmic goître treated by this

method. In 36 cases improvement of varying degree occurred; in 25 there was no improvement, and in 1 there was an aggravation of symptoms, resembling in all respects that commonly caused by thyroid feeding in this disease. In one of the unimproved cases a combination of thymus and thyroid was employed at first, and later the thymus alone was given until a few days before death.

In the cases of improvement the effect upon the more characteristic symptoms was as follows:

Exophthalmos: the exophthalmos disappeared in 8 cases; in 1 it nearly disappeared; in 8 it was diminished in amount; in 1 it is stated that the patient was practically cured; in 6 the symptom is not mentioned; and in 12 there was no effect.

Goître: in 4 cases a slight enlargement of the thyroid gland disappeared; in 12 the size was reduced; in 13 there was no effect; in 7 the goître is not mentioned.

Pulse-rate: in 17 cases the pulse-rate was reduced; in 3 of these the reduction was very slight. In 13 cases there was no diminution in the frequency of the pulse; in 6 cases the symptom is not mentioned.

In a large proportion of the 36 cases it is evident that there was an improvement in the subjective sensations, and in many in the general condition, including a gain in weight. In the remaining 26 of the 62 cases either no beneficial effect was observed or an aggravation of symptoms occurred.

It is desirable to compare the favorable results which have been described with those obtained by other methods of treatment.

McKenzie[29] has carefully contrasted twenty cases of exophthalmic goître personally treated by him with thymus preparations, either alone or combined with other remedies, with a similar number also personally treated by other methods. As regards the pulse-rate, "there was nothing in favor of the thymus treatment." The goître became materially smaller in three cases under thymus treatment; in two it increased, and in another it increased after first diminishing. In the remaining cases it remained practically unchanged.

In the *contrast*-cases the goître diminished in four; in a fifth it entirely disappeared; in one case it increased; in the remainder no change was observed. Under the *thymus* treatment proptosis decreased distinctly in only one case, and in this instance a reduction had begun before the thymus was given. In the *contrast*-cases the exophthalmos disappeared in three.

McKenzie's conclusions are that the thymus gland possesses no specific action in exophthalmic goître; that "in most cases it has no effect upon the heart, goître or proptosis." At the same time he believes it to be "a remedy of some value, improving the general condition, and in this way assisting toward recovery." He places it in the same class of remedies as cod-liver oil.

In two severe cases carefully observed from day to day in my hospital wards for the past five months, in which the thymus treatment alone was used for months, and other methods subsequently, the former treatment was without the slighest beneficial effect upon any symptom. In one the thyroid increased by an inch during the thymus period. In contrast, in one of these cases there was marked improvement in the tremor, a diminution in the pulse-rate, a reduction in the goître of an inch, with improvement in the general condition, accompanying the use of bromides and belladonna, to be followed again by a recrudescence of the symptoms.

Maude,[30] in reporting four cases treated with marked benefit with thymus preparations, remarks that he "cannot claim that the rapidity and maintenance of improvement have been more than might occur under other treatment, or none at all."

In judging of the therapeutic value of the thymus treatment in exophthalmic goître too much reliance should not be placed upon the relative number of published cases of successes and failures. Favorable results from a new remedy are more frequently reported than failures.

Finally, in few diseases is it as difficult to speak positively of the value of any particular method of treatment. The natural fluctuations of the disease are great, and improvement and recrudescence occur often in an unexplainable manner.

Goître. Mikulicz[31] has reported thirty cases of goître treated with thymus extracts. In twenty cases the goître underwent a decided reduction, as ascertained by exact measurements, and subjective improvement followed. Among these are several cases which had only slightly improved or which had become worse under thyroid treatment. A complete cure in the anatomical sense was only obtained in two cases. With the exception of one case (mixed nodular and diffuse parenchymatous) they were all diffuse hyperplastic tumors. Five of the unsuccessful cases were of the nodular and five of the diffuse hyperplastic form.

The mode of action of the remedy remains a matter of speculation. It is possible that the active principle is an iodine compound, which

Baumann was able to isolate in the case of the thymus as well as the thyroid gland.

In view of the possible stimulation of the nutritive processes in exophthalmic goître by the thymus extracts, it is of interest to study their effects in other diseases attended with impaired nutrition.

With this object in view the treatment was tried in my hospital wards during the past winter in six carefully selected cases of apyretic pulmonary phthisis.

The general condition, weight, and physical signs of the patients were carefully noted for a period before the institution of the thymus treatment. The extract in daily doses of 45 grains, speedily increased to a drachm, was then given continuously for two months, when the usual treatment of the hospital—creosote, the malt preparations, and cod-liver oil—was resumed.

In Case I. (infiltration of one apex) the weight, which had been nearly stationary, increased two pounds during the first three weeks of treatment, there was a loss of six pounds during the subsequent five weeks, when the usual treatment was resumed.

In Cases II. and III. (consolidation at one and at both apices respectively) the weight was stationary prior to treatment. There was a gain of four pounds in each case during the first three weeks, and then a loss of eight pounds in one case and two pounds in the second case in the subsequent five weeks. In the following two months, under ordinary treatment, in the case showing the greatest loss, there was a gain of two pounds; in the other there was no gain.

In Case IV. (consolidation at both apices) there was a gain of two and one-half pounds in the first two months, and then a loss of three and one-half pounds in the succeeding two months under other treatment.

In Case V. (infiltration at one apex) a gain of seven pounds in three weeks was followed by a loss of four in the succeeding five weeks, which was again followed by a gain of two pounds in the seven weeks subsequent to the discontinuance of the thymus.

Finally, in Case VI. (consolidation at both apices) there was a gain of a pound in the first week, and a continuous loss, amounting to eight pounds, from this time until other treatment was substituted for the thymus. In five of the six cases it is seen that an increase in weight occurred during the first weeks of treatment. The gain was followed by a loss, varying in amount. In only one case was there no loss in weight during the two months of the thymus treatment.

In all the cases there was little or no change in the general condition and physical signs during the thymus treatment, although at first, as is so often the case with the trial of a new remedy with the knowledge of the patient, expression of improvement in subjective sensations was made.

Whether the favorable response in the first weeks to the remedy, as shown in improved nutrition, may not be referred to the stimulus of hope, permits of speculation.

Pituitary Body. As in the case of the glandular structures already considered, the function of the pituitary body is variously believed to be of a secretory or excretory nature.

Schaefer and Oliver's[32] experimental investigations with decoctions of its tissue indicate that its activity is of a secretory character.

Rapid and great rise of blood-pressure was observed, and it was shown that the action of the active principle was a direct one upon the arterioles and probably so upon the heart-muscles. They conclude from their results that the pituitary body furnishes a secretion to the blood which serves to increase the contractile power of the heart and arteries and to influence the nutrition of certain tissues.

On the other hand, very slight physiological effects, beyond a slight elevation of temperature, slight depression, and some gastro-intestinal disturbance accompanied by emaciation, were noted by Mairet and Bosc in their experimental work.[33]

Marie,[34] who first described the disease acromegaly, regarded by many as dependent upon pathological changes in the pituitary body, believes that the function of the gland is to neutralize or destroy certain toxins whose accumulation in the blood provokes a hyperplasia of connective tissue, including the bony structures.

On the basis of a presumable glandular activity, the use of preparations of the pituitary body has been suggested in acromegaly.

With few exceptions autopsies in cases of this disease have shown macroscopic lesions of the pituitary; they have consisted chiefly in simple hyperplasias of its structures or of tumors of various kinds with or without apparent change in the volume of its glandular tissue. Tamburini[35] has recently collected twenty-four autopsies, in which tumor existed in seventeen, and of the remaining seven he considers the diagnosis of acromegaly to be doubtful in five. In the case of either lesion it is presumable that the function of the gland is affected. Both diminished secretion and hypersecretion have been suggested in explanation of the evolution of the symptoms of acromegaly. Clinical as well as pathological observations

may be urged with equal force in favor or in disproof of either of these theories. From the standpoint of pathological anatomy, it may be said that while destructive lesions are the exception, they do occur; and in cases of tumor the absolute volume of the proper tissue of the gland, whether increased or diminished, affords no reliable indication of its functional activity. Experimental reduction of the volume of glandular tissue (Gley[36]) fails to support the theory of secretory failure.

Clinically, in a few cases the administration of pituitary extracts has been found to relieve certain of the characteristic symptoms, a result which does not harmonize with the hypersecretion theory; and yet such a result is not necessarily incompatible with it. Still less does it negative the possibility of a hyperactivity of one element in a composite function, the product of which may not be present in the preparation as actually administered.

Marinesco has advanced the hypothesis that some perversion occurs in the composition of the secretion, or that some lack of balance arises between it and the products of the other ductless glands, as a result of which nervous control over the nutritive processes is impaired. In this way provision is made for including both the hypertrophic and the atrophic lesions of the gland.[37]

The idea of a correlated activity of several of the glands jointly influencing nutrition, either directly or through the medium of the nervous system, is sufficiently elastic to cover almost any combination of circumstances; but it must be remembered that it is as yet an unproved hypothesis.

Arnold,[38] Dreschfeld,[39] and Dercum[40] go one step further and favor a primary nervous lesion of unknown character, thus reducing the glandular changes to phenomena of the second order.

In conclusion, it may be said that while the whole subject presents an accumulation of theories having an exceedingly slender support on definite findings, it is probable that the pituitary gland bears some unascertained relation to the nutrition of bony and dermal tissues, as a result of which an overgrowth of them accompanies changes in the gland which presumably affect its functions. Whether these changes are primary is as yet unknown.

A few cases have been reported which indicate a widespread involvement of the glands of internal secretion and suggest a possible common origin. Murray[41] has collected five cases of this kind; in all acromegaly and exopthalmic goître co-existed, and in four glycosuria also was present, pointing, perhaps, to some per-

version of the pancreatic secretion. In the two cases with fatal issue the thyroid and pituitary glands were enlarged, and in one of these the thymus was persistent and hypertrophied.

I have collected thirteen cases of acromegaly treated with pituitary preparations. In seven cases varying degrees of improvement were noted. In one of these the improvement occurred under the combined use of pituitary and thyroid preparations. In five cases no effect was obtained; and in one case the patient was made worse by the treatment.

In two cases of improvement the violent headache and neuralgic pains in the limbs were diminished, and the general condition otherwise improved. There was no diminution in the size of the affected tissues.

In a third case the general condition was improved; no painful symptoms had been present at any time.

In a fourth case, after fourteen days of treatment the patient was able to approximate the teeth better than before, and the patellar reflex on the left side, which had been absent, was restored. Under treatment with thyroid extract for several months previously no improvement had occurred.

In a fifth case it is stated that the patient had greatly improved under treatment.

In a sixth case the patient was treated for two months with thyroid preparations, then for three to four months with pituitary extract, and finally for one and one-half months with combined pituitary and thyroid preparations. The final result was a decided decrease in the measurements of the extremities, an almost complete disappearance of the neuralgic pains, and an improvement in the general condition.

Finally, in the seventh case, there was an improvement in the mental condition.

A tabular report of these cases is appended.

Adrenal Preparations in Addison's Disease.

Observer.	No. of cases.	Results.	Remarks.
Blackader, A. D., Montreal Med. Journ., Nov. 1893, and results from personal letter.	1	Distinct improvement.	Under treatment four weeks; energy and power of endurance greater; bronzing of skin less marked.
Chauffard, La Semaine Méd., 1894, p. 74.	1	Not improved.	
Abelous, Langlois, and Charrin, Arch. de Physiol., 1892, p. 721.	1	Not improved.	Patient profoundly tuberculous; death followed in a short time.
Sée (Germain). quoted by Abelous, Langlois & Charrin, Arch. de Physiol., 1892, p. 721.	1	Not improved.	Death shortly after from general tuberculosis.
Langlois, Bra. Methode	1	Improvem't in asthenia	Passed out of observation at end of one month.
Brown-Séquard, p. 536. Presse Méd., 1896, p. 1181.	1	Not improved.	Patient soon declined to be treated on account of pain at seat of the injections.
Lloyd-Jones, Brit. Med. Journ., 1895, ii. 483.	1	Improved.	
Francis, Brit. Med. Journ., 1896, i. 1088.	1	General improvement; cutaneous pigmentation lessened; pigment in mouth unchanged.	Improvement continued for several months, followed by relapse and death.
Dyson, Quart. Med. Journ., 1894, iii. 43.	1	Not improved.	Very advanced case.
Sansom, Brit. Med. Journ., 1895, ii. 1235.	1	Improved.	"Subjective symptoms improved wonderfully." Treatment was irregular, and at date of report patient was relapsing.
Althaus, Brit. Med. Journ., 1895, ii. 1235.	1	Improved.	Improvement only temporary, followed by death.
Stockton, Med. News, 1895, lxvii, 551.	1	Cured.	Pigmentation almost removed, and general condition practically restored to normal.
Murrell, Lond. Lancet, 1896, i. 289 (also Parkinson, Brit. Med. Journ., 1896, i. 150).	1	Not improved.	Asthenia and pigmentation three months; under treatment for the following six weeks, at the end of which death occurred.
Shoemaker, Univ. Med. Mag., Feb. 1895, p. 309.	1	Improved.	Subcutaneous injections of glycerin extract for two months. Subjective symptoms restored to normal, pigmentation about as before.
Turney, Brit. Med. Journ., 1896, i. 150.	2	Not improved.	Very advanced cases. One patient lived only two days; the other only two weeks.
Oliver (Thomas), Internat. Clinic, 1894, ii. 23.	1	Not improved.	
Ringer and Phear. Clin. Soc. Trans., xxix. 68.	1	Improved.	Asthenia and pigmentation improved until the end of the fourth week, when the appetite failed, and treatment was suspended. The patient died two weeks later.

Observer.	No. of cases.	Results.	Remarks.
Tonoli, Gaz. Med. Lomb., xlv. 321.	1	Cured.	Treatment with powdered adrenal tissue for two months.
Shattuck, report by Cabot, Med. News, 1896, lxix. 281.	1	Apparently well.	Has remained apparently well for four months.
Stewart (T. G.), rep. by Duckworth, 20th Cent. Pract., ii. 24.	1	Not improved.	
Spillmann, Rev. Méd. d.l'Est., 1896, xxviii. 44. Rev. des Sci. Méd., 1896, xlviii, 86.	3	2 not improved.	
		1 improved.	Subsequently relapsed.
Osler, Internat. Med. Mag., Feb. 1896. Johns Hopkins Bul., 1896, p. 208.	1	Markedly improved.	Gained weight, strength fully restored, pigment has disappeared from palate, but not changed on integument. Eight months after the original report the patient, who has meanwhile been treated without much regularity, is said to be failing rapidly.
	1	Not improved.	Died on the seventh day of treatment.
Oliver (George), Brit. Med. Journ., 1895, ii. 561, 653.	1	Practically well.	Last report at end of twelve months' treatment. This case also reported by Rolleston and by Oliver several times.
	2	Markedly benefited.	One still under treatment at last note, the other lost sight of.
Wood, Univ. Med. Mag., viii. 483.	1	Apparently well.	Immediate improvement in subjective symptoms, after a few months apparently well; bronzing not affected.
	(2 or 3)	(Improvement.)	(Author states that he knows of these cases; no details.)
Stockman, Edin. Med. Journ., Feb. 1897, p. 211.	2	1 no improvement.	
		1 improved.	Improvement had lasted twenty months at date of report. Patient is able to follow his ordinary occupation, but relapses occur when treatment is suspended.
Maragliano, Riforma Med., 1894, iv. 650.	1	Improvement.	Subjective improvement and increase in muscular strength. Able to walk after the tenth injection (twenty days), although previously bed-ridden.
Pitrés, Cong. de Med. Int. Bordeaux, 1895,	2	Worse.	Injections caused severe local irritation and aggravation of symptoms.
Faisans, personal com. to Dupaigne, Thèse de Paris, 1896.	1	Improved.	Pigmentation improved, other symptoms persisted.
Dupaigne, Thèse de Paris, 1896, pp. 109, 118.	2	1 no improvement.	An advanced tuberculous case.
		1 improved markedly.	Improvement in pigmentation and asthenia while under treatment during three months. Died quite suddenly when treatment was suspended.
Epelbaum, Thèse de Paris, 1895.	2	1 improved.	Under treatment only a short time, and subsequently lost sight of; improvement very marked from two weeks' treatment.
		1 improved.	After two months of treatment was able to return to work.
Dieulafoy, Dupaigne, Thèse de Paris, 1896, p. 131.	1	Improved.	Improved only while under treatment; relapsed promptly each time it was suspended.
Bèclère, Dupaigne, Thèse de Paris, 1896, p. 133.	1	Cure.	Treated with ingestion of fresh gland for one month, and then for three and a half months with subcutaneous injections of extract. Pigmentation disappeared and patient was able to work. Cure had continued one year and a half at date of report, patient remaining under observation.

Observer.	No. of cases.	Results.	Remarks.
Marie, Dupaigne, Thèse de Paris, 1896, p. 136.	1	Improved.	Asthenia less marked.
Bramwell, Brit. Med. Journ., 1897, i. 67.	1	Marked improvement.	Improvement lasted for a year, when death occurred. Asthenia improved so that the patient shortly before his death was able to walk eight miles.
Quine, Journ. Amer. Med. Ass., 1896, xxvi. 1012.	1	No improvement.	Treatment only continued twelve days; patient died four days later.
Darier, Ann. de Derm. et d. Syph., 1895, p. 464. See also for termination, Dupaigne. loc. cit. p. 102.	1	No change.	Treatment suspended on fifteenth day on account of local abscess. He died soon after.
Schilling, Münch. med. Woch., 1897, p. 170.	1	Improved.	Three months' treatment; weight rose from 69-99 lbs. Strength fully restored, bronzing markedly diminished. Died three months later with toxæmic symptoms.
Kinnicutt (unpublished case).	1	No effect.	Treatment initiated only with the development of toxic symptoms. Death five days later. Diagnosis confirmed by autopsy; general tuberculosis, tuberculous and fibroid changes in adrenals.

Thymus Therapy in Exophthalmic Goitre.

Observer.	No. of cases.	Results.
Owen (Brit. Med. Journ., 1896, vol. ii. p. 1017)	3	Improved.
Williams (Clinical Journ., vol. vii. p. 93)	1	Worse.
Cunningham (Med. Record, vol. xlvii. p. 742)	3	Improved.
Taly-Guerin (Sem. Méd., 1895, p. 331)	1	Not improved.
Solis-Cohen (Philadelphia Polyclinic, 1896, vol. v. p. 446)	4	Improved.
Dreschfeld (Practitioner, 1896, vol. lvii. p. 154)	3	Not improved.
Todd (Brit. Med. Journ., 1896, vol. ii. p. 195)	1	Improved.
Maude (Lancet, 1896, vol. ii. p. 173)	4	Improved.
McKee (Brit. Med. Journ., 1896, vol. i. p. 656)	1	Improved.
Edes (Boston Med. and Surg. Journ., 1896, vol. cxxxiv. p. 82)	1	Improved.
Mikulicz (Centrbl. f. Chir., 1896, p. 929)	8	1 improved. 7 not improved.
Parker (Brit. Med. Journ., 1897, vol. i. p. 528)	1	Improved.
Lockie (Brit. Med. Journ., 1897, vol. i. p. 529)	2	Improved.
Sutcliff (Brit. Med. Journ., 1897, vol. i. p. 782)	1	Improved.
Metcalf (rep. by Mackenzie, Amer. Journ. Med. Sci., 1897, 132)	2	Improved.
Mackenzie (Amer. Journ. Med. Sci., 1897, p. 132)	20	13 improved. 7 not improved.
Booth, J. A. (personal communication)	4	Not improved.
Kinnicutt	2	Not improved.

Pituitary Treatment of Acromegaly.

Observer.	No. of cases.	Results.	Remarks.
Bard, Lyon Méd., 1892, lxix. 547	1	No result.	Pituitary extract from rabbit used subcutaneously. Author proposed to continue the treatment with extract derived from ox and sheep, but no further report can be found.
Marinesco, Bull. et Mém. Soc. Méd. des Hôp., 1895, p. 715	2	Very much improved.	The violent headache and neuralgic pains in the limbs considerably reduced, and the general condition otherwise rendered more satisfactory. No diminution in size of diseased parts. Marked diuresis. Author believes that the treatment exercised an effect either on the pituitary tumor or the cerebral circulation.
	1	Slight improvement.	General condition improved. This patient did not present any painful symptoms.
Mendel, Berl. klin. Woch. 1895, 1129.	1	Improved.	After fourteen days' treatment patient was able to approximate the teeth better than before, and the patellar reflex on the left side, which had been absent, was restored. This case had been treated for several months with thyroid extract without improvement.
Bramwell, Brit. Med. Journ., 1894, i. 21.	1	Improved greatly.	Author states that improvement may have been due to favorable general conditions during hospital residence. Previous treatment with thyroid had failed in this case.
	1	No effect.	Subsequently improved under thyroid.
Thomas, Brit. Med. Journ., 1896, i. 909.	1	No effect.	Refused to continue treatment because it made her "feel queer." Subsequently relieved by trephining.
Dinke, N. Y. Med. Record, 1896, l. 779.	1	Marked improvement.	Treatment for two months with thyroid, then for three to four months with pituitary, and finally for one month and a half with thyroid and pituitary combined. The final result was a decided decrease in the measurements of the extremities; pains had almost disappeared, and the general condition was improved. Patient believes that the improvement was due to the thyroid.
Osler, Prin. and Pract. of Med. (1895), p. 1047.	1	Not improved.	
Broadbent, Dodgeson, Lancet, 1896, i. 846.	1	Some improvement.	Chiefly in the mental condition; possibly due to the relief of the obstinate constipation.
Rolleston, Lancet, 1896, i. 1137.	1	No improvement.	Measurements increased. Author attributes the relief in pains and diminution of glycosuria to rest and diet.
Schultze, Berl. klin. Woch., 1896, p. 407.	1	Worse.	Caused irregularity of heart-action, and death followed.

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INTERNAL SECRETIONS CONSIDERED IN THEIR PHYSIOLOGICAL, PATHOLOGICAL AND CLINICAL ASPECTS.

Sporadic Cretinism in America.

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2. RESULTS OF THE THYROID TREATMENT.
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I. INCIDENCE OF THE DISEASE IN AMERICA.

In 1893 I made a collective investigation on the subject of sporadic cretinism in this country, and was able to find only 11 cases. Since that time the profession has learned to recognize the condition, and I am able to-day to report upon 60 cases, including those already referred to. Of these 27 have been reported; for the others I am indebted to various physicians throughout the country who have kindly responded to my inquiries, and in many cases sent photographs.

The following cases have been reported in full in the American Journal of the Medical Sciences, Nov. 1893, but it will be interesting here to report on their progress since that date.

Series I.

Case I.—M. ——— has been under observation from Jan. 10th, 1892, at which time she was two years and three months old, and presented a typical picture of infantile myxœdema. I reported upon her case in the February number of the Archives of Pediatrics for 1895. The thyroid extract was started in March, 1893, and she grew four inches in the first fourteen months. She learned to walk and talk, ran about everywhere, and lost altogether the cretinoid appearance. I have seen this child at intervals of a few months ever since. She has continued to take the thyroid extract, and has

grown and developed, and now nothing whatever peculiar is to be noticed about her.

Case II.—A cretinoid imbecile, nineteen years old at the time of observation, March 3d, 1893, without any special evidence of myxœdema. She has a goître in which the left lobe is more enlarged than the right. This patient took thyroid extract at intervals for some time without any special benefit.

Case III.—A child aged three and a half years when she came to the Johns Hopkins Hospital Dispensary, Nov. 25th, 1892, was a typical instance of infantile myxœdema. She was unfortunately lost sight of.

Case IV.—Dr. Bullard's Case, G. S., female, aged six years. Dr. Bullard writes on April 14th, 1897, "She has had no treatment, and is essentially in the same condition as when I wrote in 1893. She has grown little if at all, and is a dwarf.

Case V.—Sarah McGrath, aged nineteen years. (Dr. Brownell, New York State Custodial Asylum, Newark, N. Y.) (Fig. I.)

March 26th, 1897, Dr. Brownell writes, "Sarah McGrath died about two years since in the Erie County Almshouse, Buffalo, to which she was removed shortly after the history sent you was taken. I regret to say that I have no subsequent notes of her case." Not treated.

Case VI.—Louisa Schmidt, aged fourteen years. (Dr. Van Sweringer, Indiana School for Feeble-minded Children.) Dr. Delia Howe writes on April 14th, 1897, that the thyroid treatment was commenced in September, 1895, three grains of desiccated thyroid gland t. i. d. She emaciated rapidly and the treatment was frequently intermitted. The protruding abdomen disappeared, but the patient did not gain in height, and her features were not much changed. She became much brighter mentally. The treatment was stopped in March, 1896, as the patient's physical condition was very poor. She died of acute tuberculosis in November, 1896. Height at time of death, 127cm. Thyroid gland weighed 4 grms. and was degenerated. Patient died of acute tuberculosis in Nov., 1896. Case will be reported in full under pathological anatomy.

Case VII.—Martha L. Y., aged sixteen years. (Dr. J. C. Carson, Syracuse State Institution for Feeble-minded Children.)

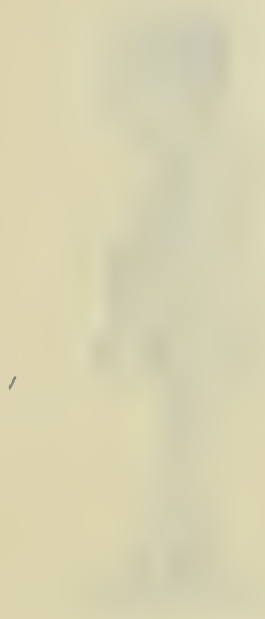


Fig. I.—Case V. (*p. 170.*) *Sarah McGrath, aged 19.* (*Dr. Brownell.*)

FIG. I.

Figs. II. a and II. b.—Case VII. (*p. 170.*) *Martha L. Y., aged 16.* (*Dr. J. C. Carson.*) *Fig. II. a shows the patient one year before and Fig. II. b one year after the administration of thyroid extract.*

FIG. II. *a*.

FIG. II. *b*.

FIG. III.

Fig. III.—Case X. (p. 171.) Nellie R., aged 15. (Dr. Furness, reported by Dr. Fred'k. Peterson.) This case shows remarkably well the infantile appearance.

The further history of this case is as follows. Treatment was begun Sept. 4th, 1895. At that time her height was 40½ inches, and the weight 57 pounds. After one month the change in her condition was striking. At the end of two months the entire skin was renewed, giving place to the velvety skin of an infant, and a new growth of hair just appearing on the head. At the end of eight months she had grown three and one-eighth inches, and weighed 62½ pounds. The teeth which have appeared since treatment are eight incisors, one canine, and two second molars. The photographs (Fig. II.) show the condition a year before and a year after treatment. *(Journal of Psycho-Asthenics, Dec., 1896.)*

Case VIII.—Willie V., aged forty-two years. (Dr. Hoisholt, State Insane Asylum, Stockton, Cal.). April 1st, 1897, Dr. Clark writes that he cannot report any material change in the condition of the patient. He has less frequent epileptic attacks, and seems to be enjoying better physical health than he did formerly. Thyroid extract had not been given on account of the age of the patient, but was commenced on the day the letter was written (April 1st, 1897).

Case IX.—Johnny V., brother of the preceding case, aged forty years. Of this patient Dr. Clark writes that he sees no change excepting that the scoliosis is more marked; he leans very much to one side when he walks. The thyroid extract had not been tried on account of the age of the patient, but was commenced on the day the letter was written.

Case X.—Nellie Roume, aged fifteen years. (Dr. Furness, Randall's Island Hospital, New York.) (Fig. III.) Dr. Frederick Peterson reports this case in *Pediatrics* for May 1st, 1896. He says, "Treatment was begun with five grains of the dried gland, which proved too much, and it was reduced to one grain daily. Improvement was noticeable in a few days. In the course of three months she grew thinner, gained two inches in height, cut several new teeth, her hair became more abundant, she assumed an intelligent expression, noticed everything about her, played with a doll, and had increased her vocabulary to twenty-seven words. At this time treatment ceased because of changes among internes and attending physicians."

Case XI.—I. N., female, aged probably thirty-five years. (Dr. A. E. Osborne, Inmate of the California Home for Feeble-minded

Children.) In a note from Dr. A. E. Osborne of April 1st, 1897, he says, "I regret to have to say that our cretin died shortly after I forwarded you the notes relating to her. I really have nothing further of material interest regarding her." Not treated.

It will be noted that of these cases six have not been treated thoroughly, three have been treated with great improvement, and two have died.

Series II.

I will first give brief notes of the three additional cases which have been under observation at the Johns Hopkins Hospital, and then in order the cases which either have been reported in the literature in this country, or the notes of which have been furnished to me for the purpose of this report.

Case XII.—J. L., aged forty-three, admitted to the Johns Hopkins Hospital, Surgical Department, for cystitis. He presented a very characteristic appearance of a cretinoid dwarf. He had a muddy complexion, dry skin, harsh rasping voice. There was no goître. He had a fair amount of intelligence, but he was in many ways infantile and childish. He received no special treatment.

Case XIII.—Theophilia Purzika, aged 2, was admitted to the Johns Hopkins Hospital Dec. 18th, 1895. It was very difficult to get a history, as the mother was a Pole and did not speak English. This is the second child; natural at birth. No goître in the family. The thyroid gland can be felt, seems a little large. She presents the typical aspects of infantile myxœdema. Though of fair size for her age, she can neither sit nor stand. The child looks pale; the skin of the face has a sallow, waxy appearance. The tongue is large, held out all the time. The expression of the face is dull and idiotic. The lower jaw drops, and she drools constantly. There are eight incisor teeth, and she is cutting a lower molar and the molars of the upper jaw. The eyelids are puffy and the palpebral orifices look narrow. The skin of the face is rough, and there is a puffiness and myxœdematous character of the skin of both hands and face. The head measures 45cm. in circumference, 25½cm. in the transverse, and 35cm. in the antero-posterior. The anterior fontanelle is large, almost as much so as at birth. The posterior fontanelle is completely closed.

Figs. IV. a and IV. b.—Case XIII. (*p. 172.*) *Illustrate the effect of two months' treatment.*

FIG. IV. *a*.

FIG. IV. *b*.

FIG. V.

Fig. V.—Case XV. (*p. 173.*) *A remarkable example of a pregnant cretin.* (*Dr. Townsend.*)

The abdomen is large and pendulous. The skin of the thighs, as shown in the photograph, hangs in folds. Her length on admission was 65cm. The blood count gave 4,648,000 red corpuscles, 80 per cent. of hæmoglobin, and about 11,000 leucocytes.

On Dec. 20th she was placed on the thyroid extract prepared by Dr. Abel. On commencing the treatment she weighed twenty pounds. Within two months, as illustrated in the photograph, (Fig. IV.) the condition improved remarkably. She took an interest in surrounding objects. The eyes had become bright and intelligent; the puffiness of the face and hands had almost wholly gone. As shown in the photograph, the palpebral orifices had grown much larger. The tongue was not held out so far from the mouth, and the drooling had almost ceased. She remained in the hospital until Sept. 1st, 1896. The myxœdematous condition disappeared entirely, she gained eight pounds in weight, and had thriven very well. It is interesting to note in this case that from the 20th of March to the 4th of April the child received no thyroid extract. She had had a little fever and bronchitis and it was stopped. On the latter date it was noticed that the skin had become harsh and dry, the eyelids more puffy, and the child did not seem nearly so well.

Case XIV.—Teresa Teichman, aged 2, brought to the Johns Hopkins Hospital Dispensary April 9th, 1896. The parents are Poles. Child at birth was natural. She has never walked or talked; cannot stand alone. She is very apathetic, but seems to understand everything. The mouth is held wide open. The tongue does not protrude. The face is broad; the eyelids are puffy; the nose is broad, the orifices of the nostrils very plainly to be seen. The mouth is large, the lips full, and the cheeks flabby and relaxed. There is a waxy sallow tint to the skin. The head is broad, parietal eminences marked, forehead low. The tongue is large; upper and lower incisors are just appearing. The subcutaneous fat over the body is abundant. There are no pads above the clavicles. The belly is very prominent and pendulous. The general cretinoid aspect is most marked. The thyroid gland cannot be felt. There is no dullness over the manubrium.

Case XV.—Dr. Townsend's Case of Pregnant Cretin. (Fig. V.) No note of thyroid treatment. No note of condition of thyroid gland. Aged 38 years. Cæsarean section: recovery. *(Archives of Pediatrics, January, 1897.)*

Case XVI.—Dr. Townsend's Case. Female, seen April, 1891, aged one year and eight months. Not treated with thyroid extract. Patient died in summer of 1891 of some intestinal trouble. No thyroid gland felt. *(Arch. of Pediat., November, 1892.)*

Case XVII.—Dr. Townsend's Case. Walter McGuire, aged four years. Treatment begun Nov., 1896. Marked improvement within one month. Has grown two inches in height since beginning of treatment; no teeth before; now has four lower incisors, two lower anterior molars, and one upper anterior molar. Is very active and takes an intelligent interest in things. Can walk. Tongue smaller and kept in mouth. Treatment being continued. No note of condition of the thyroid gland. *(Not yet published.)*

Case XVIII.—Dr. Friend's Case. Hattie G., aged sixteen years and one month. (Fig. VI.) Treated with thyroid extract for one year and ten months; begun about May, 1895; much improved. Within six months the swelling had all disappeared. At the end of seven months seventeen teeth of second dentition appeared. The height increased from 76.5 cm. to 105 cm. Treatment continued almost to time of death. Thyroid gland appears normal. At the autopsy the only cause of death manifested was two drams of bloody fluid in the lateral and fourth ventricles of the brain. All of the veins were surcharged with blood, and the dura, extending about one half inch on both sides of the longitudinal sinus, was of a deep red color. The other organs showed a negative condition. The thyroid gland was absent. The thymus was very large and weighed 64.0 grams. The pituitary gland was very small, and weighed 0.2 grams. Microscopically all organs showed an excess of connective tissue. In the posterior wall of the bladder was imbedded a concretion about the size of a dime. *(Not yet published.)*

Case XIX.—Dr. Peterson's Case. M. P., male, aged eighteen months. Treatment begun June, 1895. Under treatment with the thyroid extract for ten months, at the end of which time it has grown, and seems a normal child in every respect, though still having to continue the thyroid extract. Thyroid gland small and hard. *(Pediatrics, May 1st, 1896.)*

Case XX.—Dr. Peterson's Case. Dwarf cretin, supposed to be between sixty and eighty years. Two weeks of thyroid treatment made no perceptible impression except to improve the temperature and circulation. Thyroid gland perceptible but very small.

Fig. VI.—Case XVIII. (*p. 174.*) *Female, aged 16.* (*Dr. Friend.*)

FIG. VI.

FIG. VII. *a*.

FIG. VII. *b*.

Figs. VII. a and VII. b.—Case XXI. (*p. 175.*) *Male, aged 32. Illustrating a very typical condition of advanced cretinism.* (*Dr. Lloyd.*)

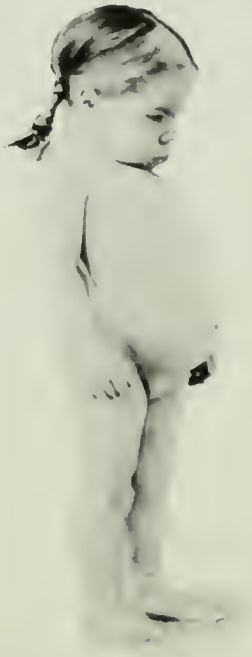


FIG. VIII. *a*.

FIG. VIII. *b*.

Figs. VIII. a and VIII. b.—Case XXIV. (*p.* 175.) *Female, aged 9.* (*Dr. Dickson L. Moore.*) *Fig. VIII. b shows the remarkable change after seven months' treatment.*

Case XXI.—Dr. Lloyd's Case. B. M., male, aged thirty-two years. (Fig. VII.) Thyroid gland of the sheep partially cooked was tried, but the patient took such a disgust to it that it was discontinued. He lost appetite and grew thinner, but no other effect was noticed. Thyroid gland entirely absent. (*International Clinic, Phila., 1892, 2d s., Vol. II.*)

Case XXII.—Dr. Herrick's Case. E. M., female, aged four years and nine months. After twelve months treatment with the thyroid extract there was marked improvement. Treatment begun Jan., 1896. She lost in weight, increased rapidly in height, and grew very bright mentally. Thyroid gland not to be seen or felt. *(Arch. of Pediatrics, April, 1897.)*

Case XXIII.—Dr. Noyes' Case. Winifred P., aged two years. Thyroid gland was palpable. Under treatment with thyroid extract for five and a half months with wonderful improvement. Treatment begun Sept. 15th, 1895. She became very bright and intelligent, and one could not notice anything peculiar about her. She gained eight inches in height. *(N. Y. Med. Jour., Mar. 14th, 1896.)*

Case XXIV.—Dr. Dickson L. Moore's Case. Eva Swanson, female, aged nine years. (Fig. VIII.) No note as to the condition of the thyroid gland. Under treatment for seven months, with the most marked improvement. Treatment begun Aug. 12th, 1896. She has gained four inches in height; the whole mental condition has changed, and she will shortly be sent to school. *(Columbus Med. Jour., April 13th, 1897.)*

Case XXV.—Dr. Fernald's Case. Female, aged four and a half years. Typical cretin. Weight 28½ pounds; height 2 ft. 4 in. Put on thyroid treatment Jan. 1st, 1897. At the end of two months she has lost two and a half pounds, and seems somewhat improved. The hair has become soft and fine, and the stupid expression is gone. At the end of four months the weight is 22½ pounds, and she is much improved. The face looks like that of a normal child. She notes everything going on about her; her vocabulary has increased and she plays intelligently.

Case XXVI.—Dr. Roger's Case. (Minnesota School for Feeble-minded, Faribault, Minn.) Gertie N., aged nine years, no sign of thyroid gland, height 34 inches, weight 32 pounds. Apparently

FIG. IX. *a*.

FIG. IX. *b*.

FIG. X.

Fig. X.—Case XXXIV. (*p. 177.*) *Goitrous cretin; female, aged 27.* (*Dr. Kessel.*)

Case XXXI.—Dr. Dercum's Case. W. H., gives his age at one time as 35, at another as 47. History obtained from the patient himself, and is of doubtful value. He is decidedly dwarfed—4 ft. 5 in. in height. The abdomen is large. There is excessive lordosis. The skin has a dirty yellowish hue, and everywhere over the body is much wrinkled, and feels harsh, dry and thick. The head is large, the face broad, the eyes widely separated, the nose short, broad, and flattened. Mentally the patient is at a level of a middle grade idiot. No thyroid gland can be felt. There is no note of treatment. *(Phila. Hosp. Reports, 1893, II, 157, 1 pl.)*

Case XXXII.—Dr. Leszynsky's Case. Male, aged twenty-five years; absence of the thyroid gland. Patient was treated with the thyroid extract without any amelioration of his condition. *("The Post Graduate," 1894.)*

Case XXXIII.—Dr. West's Case. N. R., female, aged 1 year and 5½ months; thyroid gland cannot be felt. Under treatment with the thyroid extract she improved steadily and rapidly, and at the end of six months had gained four inches in height. The mental improvement was very marked. Treatment begun July 6th, 1894.

On April 1st, 1897, Dr. West writes, "There is very little new to tell concerning her. She grows very slowly and learns to talk still more slowly. Large doses of the thyroid, i. e. enough to cause fever, restlessness, etc., for a few days, always cause a change for the better with her." *(Arch. of Pediatrics, May, 1895.)*

Dr. J. Herbert Darey, of Northwood, Iowa, called my attention to the occurrence of two cretins in the State (at Kendallsville, Winnesbrick Co.). The father was from Ulster, Ireland. His sister had enlargement of the neck. He and his wife were in no way related. They had five children, one of whom died at the age of eight months of diphtheria. Three of the children had goître, one of whom died at the age of eight years, following an operation on the goître.

The history of the cases as sent by Dr. Kessel are as follows:

Case XXXIV.—Elizabeth L., female, aged 27, height 4 ft. 7 in.; weight 100 pounds. (Fig. X.) Talks but little, but is smiling and in much better spirits than the boy. Head large. Strabismus. Health apparently good. Hears watch only on contact with both

FIG. XI.

FIG. XII. *a*.

FIG. XII. *b*.

Figs. XII. a and XII. b.—Case XLII. (*p. 179.*) *Male, aged 6.* (*Dr. Vinke.*) *Fig. XII. b shows the remarkable change five months later.*

The chronic constipation has disappeared, the mother saying, 'she hasn't given her a nickel's worth of castor oil in two months;' the appetite is enormous. Her mental state has improved wonderfully. She is brighter and far more observing, but much more difficult to manage. She has grown mischievous and quarrelsome. The speech is somewhat more distinct. She has grown one and one-half inches, and is now 35½ inches tall, and her mother had to buy her larger shoes about a month ago. On Saturday (April 10th) when I last heard from her she was reported as having walked a few steps alone for the first time." Thyroid gland not enlarged. *(Medical Review, St. Louis, Jan. 9th, 1897.)*

Case XL.—Dr. Smith's Cases. (Illinois Asylum for Feeble-minded Children). Freda R., aged 12, born in Switzerland. No goître, cannot sit up, cannot talk, tongue large and protruding, hair thin and scattered. Photograph shows evidently a general myxœdematous condition. At present under thyroid treatment. *(Private Communication.)*

Case XLI.—Richard R., a brother of the first case, aged three years, born in Chicago; three normal children intervened between the birth of these two. No goître, tongue protrudes, cannot sit up, cannot talk. At present under thyroid treatment. *(Private Communication.)*

Case XLII.—Dr. Vinke's Case, male, aged six years, first seen Sept. 2d, 1895, a typical cretin. (Fig. XII.) Patient was at once placed upon thyroid treatment, and at the very outset began to improve. At the end of two months he had lost twenty-two pounds, and gained over an inch in height; the skin became soft, warm, and natural, and he took a lively interest in his surroundings. At the end of five months, when the second photograph was taken, the change was most remarkable; the patient had now a healthy appearance, and his face was intelligent and natural. On April 9th, 1897, Dr. Vinke writes, "This little patient is still under thyroid treatment and is making most satisfactory progress. He has now taken uninterruptedly 15 grs. thyroid extract a day for the past year and seven months. During this time he has grown nine inches and his mental condition has improved correspondingly. His parents intend to send him to school now." *(Med. News, 1896, LXVIII, 309.)*

Case XLIII.—Dr. Delia Howe's Case (Indiana School for Feeble-minded Youth). Bessie Patterson, aged five years and six months at beginning of treatment. Thyroid gland not to be felt. Height 29½ inches. Thyroid treatment was begun October, 1895, grs. 3 to 5, t. i. d. Treatment has been intermittent on account of toxic symptoms. There has been marked improvement in the intervals of treatment; that is, the improvement is not marked during the period of taking the remedy, but as soon as the latter is stopped, the child makes a marked advance. At the end of eighteen months treatment she has grown 6¾ inches, and now at seven years of age she measures 36¼ inches. She is now a remarkably well-formed child, the change in every respect being almost marvelous, Mentally she is much improved; is very observant and imitates well, but does not talk. *(Private Communication.)*

Case XLIV.—Dr. Delia Howe's Case (Indiana School for Feeble-minded Youth). Willie Huff, aged six and a half years. Thyroid treatment begun Dec., 1896. At the end of four months the improvement is very marked. The mental improvement is greater than the physical. He is growing rapidly and becoming straighter. *(Private Communication.)*

Case XLV.—Drs. Jacobi and Fruitnight's Case. Male, aged 4 years; a typical cretin. Height 25 inches. (Fig. XIII.) Thyroid gland not enlarged. Treatment with the thyroid extract commenced Oct. 2d, 1895. At the end of a month he seems more intelligent and does not protrude the tongue constantly. At the end of two months the improvement is marked, both mental and physical. Notes taken at intervals from this time until the present show a steady improvement, and measurement on March 2d, 1897 shows that he has gained five and half inches in height. He says many words plainly, and can walk a little. *(Pediatrics, 1896.)*

Case XLVI.—Dr. Elsner's Case. Female, aged fifteen months at beginning of treatment. Typical cretin. (Fig. XIV.) Thyroid treatment begun in July, 1894, and within three weeks there was decided improvement of all the symptoms. In August, 1895, thirteen months after the beginning of treatment, the photograph shows a perfectly natural child, and in his letter of April 20th, 1897, Dr. Elsner writes, "She has remained perfectly well since that time, and is now in her fifth year. Her mental development is about equal to that of a child three years old." The child still has to have

Figs. XIII. a and XIII. b.—Case XLV. (*p. 180.*) *Male, aged 4.* (*Drs. Jacobi and Fruitnight.*) *Fig. XIII. b illustrates the remarkable improvement which followed the use of the thyroid extract.*

FIG. XIII. *a*.

FIG. XIII. *b*.

Figs. XIV. a and XIV. b.—Case XLVI. (*p.* 180.) *Female, aged 15 months.* (*Dr. Elsner, Syracuse, N. Y.*)

FIG. XIV. *a*.

FIG. XIV. *b*.

occasional doses of the thyroid extract. No note of condition of thyroid gland. *(Private Communication.)*

Case XLVII.—Dr. J. C. Shaw's Cases. Annie ———, aged 3, seen early in 1894; never walked, but can stand; has not developed mentally. Condition quite characteristic. Height not given. Thyroid extract administered for several months with improvement in the child's mental activity. No note of condition of the thyroid gland. No goître in the parents. Case lost sight of. Dr. A. C. Brush subsequently reported, at the discussion on Dr. Shaw's paper, that the child came under his care. She had relapsed, but improved again remarkably when placed on the extract. *(Brooklyn Med. Jour., January, 1897.)*

Case XLVIII.—Female, aged 12, seen December, 1894; height 38 inches. Characteristic condition of cretinoid myxœdema. The photograph taken a year and a half after treatment shows a characteristic and remarkable change. No note of the condition of thyroid gland. No goître in the parents. *(Ibid.)*

Dr. Shaw has also reported two other cases, but they seem to me doubtful, and are not included here.

Case XLIX.—Dr. Frank S. Wade's Case. Sadie T., aged 13, a typical cretin. No note as to condition of thyroid gland. The treatment with thyroid extract was commenced about June 1st, 1896, and the improvement has been remarkable. She now walks across the floor and can say a few words. The lips are thinner, the puffiness under the eyes has disappeared, the tongue is nearly normal, and is kept within the mouth, the skin is moist, pink and healthy, and the hair is soft and moist. Her face is now quite that of a normal child. *(Private Communication.)*

Case L.—Dr. N. S. Morse's Case (Eldora Emergency Hospital, Eldora, Iowa). Myrtle A. A., aged five and a half years when first seen. A typical cretin. No note of condition of thyroid gland; the doctor says, "there seems to be no neck, i. e., head apparently rests upon or between the shoulders." Thyroid treatment was commenced early in March, 1896, and at the end of a month the improvement was remarkable; she had lost two and a half pounds in weight, and the expression of the face and the character of the skin had entirely changed. The improvement has continued, and at the present time she is apparently a perfectly healthy, intelligent

FIG. XV.

FIG. XVI.

Fig. XVI.—Case LV. (*p. 183.*) *Cretin, aged 12.* (*Dr. Jno. R. Stone.*)

FIG. XVII. *a*.

FIG. XVII. *b*.

Figs. XVII. a and XVII. b.—Case LVIII. (*p. 183.*) (*Dr. J. W. Coyner.*) *Figs. XVII. a to f show a perfectly phenomenal change which took place in this child in eleven months' treatment. I know of no set of photographs, among all that have been published on the subject in late years, which shows such an extraordinary transformation in so short a time.*

FIG. XVII. *c*

FIG. XVII. *d*.

Figs. XVII. c and XVII. d.—Case LVIII. (*p. 183.*) (*Dr. J. W. Coyner.*) *Figs. XVII. a to f show a perfectly phenomenal change which took place in this child in eleven months' treatment. I know of no set of photographs, among all that have been published on the subject in late years, which shows such an extraordinary transformation in so short a time.*

FIG. XVII. *e*.

FIG. XVII. *f*.

Figs. XVII. e and XVII. f.—Case LVIII. (*p. 183.*) (*Dr. J. W. Coyner.*) *Figs. XVII a to f show a perfectly phenomenal change which took place in this child in eleven months' treatment. I know of no set of photographs, among all that have been published on the subject in late years, which shows such an extraordinary transformation in so short a time.*

CASE LV.—DR. JOHN R. STONE'S CASE (Parry Sound, Canada). Harry H., male, aged 12 years; a typical cretin. (Fig. XVI.) Height 2 ft. 9½ inches; weight 42 pounds. As a result of six weeks treatment with the thyroid treatment he has gained ⅝ of an inch in height, the weight has decreased, the color has changed from pale to ruddy, and the skin has become soft and velvety. The intellectual powers have increased in every respect. No note of condition of the thyroid gland. *(Private Communication.)*

CASE LVI.—DR. M. A. STARR'S CASE. Male, colored, aged 11, typical appearance. Never talked freely, says single words; never had convulsions. Is imbecile, dirty, walks with wide straddle and sways. Skin thick; tongue protrudes. Hands and feet much larger than normal. Skin of legs and feet much thickened, rough and scaly. Seen Feb. 1894 and put on thyroid. In April, 1894, very much improved mentally and physically; not seen since. *(Private Communication.)*

CASE LVII.—DR. E. F. WILSON'S CASE. Bessie D., aged ten. Well until two, when it was noticed that she was not like other children. She grew up very dull and heavy and stupid. She walked with a peculiar waddling gait, not unlike that of a child of two years. She talked enough to say yes and no, and a few other monosyllables. The tongue did not hang out, but she drooled constantly. There was great enlargement of the neck, but no distinct goître. In November, 1896, the height was 32 inches; waist 24 inches; neck 13 inches. She began to take the thyroid extract in November, and at the date of Dr. Wilson's report, at the first of May, six months later, she had grown seven inches, the waist measurement had reduced from 24 to 16 inches, and the neck from 13 to 10 inches. She has lost altogether her stupid condition and appearance, and is beginning to learn rapidly and well. *(Private Communication.)*

CASE LVIII.—DR. J. W. COYNER'S CASE, male, aged 23 months. Typical cretin. (Fig. XVII.) Thyroid treatment commenced May 15th, 1896. Height 28 inches; abdomen 19 inches. Patient began to improve at once, and photographs taken at intervals show the most marked improvement. After five and a half months treatment she has grown two inches in height, and the abdomen has reduced four inches. A photograph taken after eleven months treatment shows a perfectly normal, intelligent looking child. *(Private Communication.)*

Case LIX.—Dr. Hoover, of Cleveland, has published the notes of a case, which is interesting inasmuch as the cretinoid appearance developed with a goître about the age of ten. I am not altogether certain that it really should be reckoned among the cases of infantile cretinism. The brief notes are as follows. The boy, a Bohemian, was aged eleven when seen June 15th, 1895. He was undersized for his age; had grown very little for more than a year, and during this time had not been able to go to school, though previously he had shown the ordinary capacity of children of his age. His family had noticed a gradually increasing stupidity, with the development of a goître. For more than a year he had been quite indifferent to his surroundings, and had lost all interest in his play and studies. At present he will volunteer no information about himself, and will answer no questions. When he does speak it is in a very croaking, harsh voice. The goître is large; the circumference of the neck measures 39 cm. It has been increasing rapidly for several months. The boy was placed upon the fresh extract of the sheep's thyroid, a quarter of a gland three times a day. Within two weeks there was a remarkable change. The boy looked brighter, and the circumference of the thyroid was only 33 cm. The case was subsequently lost sight of. *(Western Reserve Medical Journal, 1895.)*

Case LX.—Dr. Jacobi. Boy, aged eighteen, no goître. Characteristic evidences of cretinism, marked impairment of mental development, early closure of the anterior fontanelle. This was the first case on record in this country. *(Hospital Gazette and Archives of Clinical Surgery, Vol. IV, p. 486.)*

The clinical summary of the cases is as follows:

Sex. Males 23; females 35.

Age. Under two years, 6; from two to five years, 12; five to ten years, 12; ten to fifteen years, 10; fifteen to twenty years, 7; twenty to thirty, 3; thirty to forty, 4; over forty years, 4.

Nationality. American, white, 12; colored, 1; Polish, 2; French, 1; German, 5; Swede, 1; Hebrew, 1; Norwegian, 1; Irish, 7; English, 1; Swiss, 2; Bohemian, 1; nationality not given, 23.

Locality. There is no region in this country in which the disease is endemic, nor does it appear to be more prevalent in those districts, as in Michigan and parts of Ontario, where goître is common.

Condition of the thyroid gland. Goître was present in 7; gland stated to be normal in 12; gland small in 2; gland not to be felt in 16; no note in 20.

II. THE RESULTS OF THYROID TREATMENT.

No type of human transformation is more distressing to look at than an aggravated case of cretinism. It recalls Milton's description of the Shape at the Gates:

> "If shape it might be called, that shape had none
> Distinguishable in member, joint, or limb."

or those hideous transformations of the fairy prince into some frightful monster. The stunted stature, the semi-bestial aspect, the blubber lips, *retroussé* nose, sunken at the root, the wide-open mouth, the lolling tongue, the small eyes, half closed with swollen lids, the stolid, expressionless face, the squat figure, the muddy, dry skin, combine to make the picture of what has been well termed the "pariah of nature."

Not the magic wand of Prospero or the brave kiss of the daughter of Hippocrates ever effected such a change as that which we are now enabled to make in these unfortunate victims, doomed heretofore to live in hopeless imbecility, an unspeakable affliction to their parents and to their relatives. From a large number of photographs which I have received I have selected a set to illustrate the effect of treatment at different ages, from infancy to the thirtieth year, and illustrating also the influence at periods varying from two months to a year. The series has an educational value, as the pictures tell their own story, enabling the practitioner not only to recognize the victims of this affection, but they emphasize as words cannot the magical transformation which follows treatment.

Fig. XIV*a*, shows the patient of Dr. Elsner, of Syracuse, New York. The child was eighteen months old at the beginning of treatment, and the photograph shows a very characteristic state of infantile myxœdema. Fig. XIV*b*, shows the state thirteen months after treatment.

Fig. IV*a*, shows Case XIII. of the series. She was two years old at the beginning of treatment. Fig. IV*b*, shows the condition after two months' treatment.

Fig. XIII*a*, is a child aged four years, a patient of Dr. Jacobi and Dr. Fruitnight. The facies and general conformation are most typical. Fig. XIII*b*, shows the change a year and a half after treatment.

Fig. XII*a*, illustrates the case of Dr. Vinke, of St. Charles, Mo., a boy aged six years. Fig. XII*b*, shows the condition five months after treatment. In a year and a half he grew nine inches.

Fig. VIII*a*, shows a patient of Dr. Dickson L. Moore, of Columbus, Ohio, a girl aged nine years. The treatment was begun August 12, 1896. Fig. VIII*b* shows the condition seven months later, March 20, 1897. The child had gained four inches in height, and the entire appearance had changed remarkably.

Fig. II*a*, presents a typical picture of a sporadic cretin, aged seventeen years, under the care of Dr. J. C. Carson, of Syracuse, New York. Fig. II*a* was taken a year before treatment, and Fig. II*b* illustrates the condition a year after.

Fig. IX*a*, shows a sporadic cretin at the age of thirty years, patient of Dr. Sinkler. The height was 112¾ cm. Fig. IX*b* shows the condition a year after treatment. She had grown nearly 7 cm., and had lost much of the myxœdematous characters. This case is of special interest as showing the importance of the treatment even in adults.

I know of no single set of photographs which show in quite the same way the phenomenal change as in the following series of pictures very kindly sent by Dr. Coyner, Peoria, Ill.

Figs. XVII*a* and XVII*b*, show the very characteristic appearance of a sporadic cretin, aged twenty-three months, length 28 inches, circumference of the abdomen 19 inches. Fig. XVII*c*, shows the change after three months' treatment; the abdomen measured 16 inches. Fig. XVII*d*, illustrates the condition after five and a half months' treatment; height 30 inches; abdomen measured 15 inches. Fig. XVII*e*, shows the change after seven and a half month's treatment; while the last picture, Fig. XVII*f*, shows eleven months after beginning the use of the thyroid a perfectly natural-looking child.

1. *The character of the changes.*

(*a*) Bodily. Loss in weight, due to disappearance of the myxœdematous condition and of the fat, is noticed within a month or six weeks after the commencement of the treatment. The face becomes thinner, the palpebral orifices wider, the puffiness disappears from about the eyes, the flabby supraclavicular folds melt away, the projecting abdomen diminishes in girth, and the child's figure becomes more shapely. Several of the photographs illustrate this in an interesting manner. This change is much more striking in young children of from three to six or eight years, but it is also well seen in the older patients. Nothing could be more remarkable than the change in the features in Dr. Carson's case, and even in Dr. Sinkler's case, aged thirty years, the change, as shown in the photograph, is

most evident. The expression of the face is altered by the recession of the tongue, and in many instances the drooling ceases as the mouth is kept closed; this relieves in great part the idiotic expression.

Among the constructive and progressive alterations may be mentioned the loss of the waxy pallor of the skin, which becomes softer and much more natural-looking.

The hair, too, changes, and becomes more abundant and finer. Several writers have referred very particularly to this remarkable change in the skin and hair, as though there had been a complete substitution of the old by a new skin and hair. In very young children teething proceeds rapidly; in older subjects, if the second dentition has not begun, the milk-teeth are shed and the permanent ones develop rapidly. No change is so remarkable as the increase in stature. As Dr. John Thomson remarks, "the natural impulses of growth, which were in abeyance in the thyroidless condition, are let loose." In my first case the little girl grew four inches in a year. Among the most remarkable in the collected series are the following: Dr. Friend's case gained eleven and three-quarters inches in one year and ten months; Dr. Vincke's case gained nine inches in one year and seven months, and Dr. Noyes' case gained eight inches in four and a half months, and Dr. Edwin F. Wilson's case gained seven inches in six months.

Fig. XII, illustrates what an extraordinary alteration takes place after seven months' treatment. The loss of the squattiness of figure, the apparent disproportion between the head and the trunk, the loss of the characteristic attitude, and the disappearance of the lordosis are well illustrated. It is to be remembered that the rapidity in growth in some cases has led to increase of a lateral curvature and even to marked bowing of the legs.

(*b*) Mental change. Even within a couple of months the alteration in the mental condition is noticed. At any rate, the patients look much brighter and the face is not absolutely expressionless. This is very well seen in Fig. IV, illustrating the change after two months' treatment. As a rule, the younger the case the more marked is the mental change. Young cretins who have not learned to speak a word soon begin to talk in their play. In children between six and ten the effects are even more remarkable, and with the loss of the myxœdematous condition there is a corresponding awakening of the mental faculties. In older patients the treatment is not so efficacious. In Case II. of my series, the girl, aged nine-

teen years, did not seem to be very much benefited, although it is true the treatment was abandoned by the mother after a short time. In other instances, as in Dr. Sinkler's case, the mental condition improved very much, even though the patient was over thirty years. I know of no instance in which the treatment has benefited the condition of deaf-mutism.

2. *The dosage.* I have usually begun with a grain of the desiccated gland three times a day in young cretins. It should be carefully watched, and the amount reduced if the pulse becomes more rapid, or if there is fever. Older patients may take as much as five grains in the day, and the amount may be increased or diminished as the symptoms indicate. The cases bear the remedy very well, and in a few months, if no improvement is noted, larger doses must be tried. Unpleasant effects are less commonly seen than in the myxœdema of adults.

3. *The question of continuance of the treatment.* After the disappearance of the myxœdema and the establishment of the processes of growth and development, a very moderate dose seems sufficient, one or two five-grain tablets a week. Intermission for a month or six weeks does not seem to be followed by any striking change, but an intermission for a longer time is followed by symptoms indicating a relapse. In my first case in the early part of this year the treatment was interrupted for two months, and the child became very languid and apathetic, and improved at once when the use of the extract was renewed.

And here the thought arises: Whom has suffering humanity to thank for this priceless boon? As with many great discoveries, no one man, indeed, no set of men. The points in the development of our knowledge of the function of the thyroid gland have been worked out in almost equal shares by physicians, surgeons, and physiologists. Gull and Ord, Kocher and the Reverdins did much; but to the experimental physiologists, in particular to Schiff, to Horsley, and to von Eiselsberg, we owe directly the experimental evidence which made possible the successful treatment of myxœdema and sporadic cretinism. That I am able to show you on these lantern-slides such marvelous transformations, such undreamt-of transfigurations, is a direct triumph of vivisection, and no friend of animals who looks at the "counterfeit presentments" I here demonstrate will consider the knowledge dearly bought, though at the sacrifice of hundreds of dogs and rabbits.

III. DIAGNOSIS.

The number of cases which I have been able to collect indicates that the profession has rapidly learned to recognize sporadic cretinism. It is also evident from statements, and from photographs, which I have received, that there are a number of conditions which are apt to be mistaken, and that even men in institution life have not very clear ideas upon the subject. There are several points to which I may refer.

(*a*) *The recognition of early slight cases.* After the third year the condition is, as a rule, diagnosed at sight, and advanced types offer not the slightest difficulty. The earlier the recognition is made, the greater is the prospect of complete recovery. About the eighteenth month the subject may present the aspect of myxœdema rather than of cretinism, and the swollen, waxy skin even suggests Bright's disease. Case I. of the series was supposed to have chronic nephritis. The failure of development, the inability to talk or to walk, and the retarded dentition begin to attract attention as the child reaches this period. The absence of expression, the open mouth, the large tongue, and the drooling suggest that something is wrong. The development may be so slow that a child of three years looks not older than fifteen months. There are, possibly, cases of thyroid insufficiency in young infants which correspond to the *myxœdème fruste* of the French, which may be readily overlooked. To this several writers have recently called attention. Dr. Bury,* in the discussion last year at the British Medical Association, states that he saw a baby at a year old which had ceased to "get on." It became flabby, fat, lost his vivacity, and began to show a protuberant abdomen, a lax skin, and other cretinoid appearances. Treatment with small doses of the thyroid, one-fourth tabloid daily, speedily picked him up; he grew, became lively, and at the end of six months treatment was discontinued without retrogression. Such cases are probably due to transient, perhaps functional, disturbance in the thyroid. Herrick† also, in his recent paper, refers to the ease with which these milder cases may at first be overlooked.

(*b*) *The diagnosis from other types of idiocy.* Naturally enough it has been suggested that diminished or perverted function of the thyroid gland might be responsible for the mental and bodily defects in ordinary idiocy, and more particularly in dwarfs. The question is one deserving of careful study, particularly by those who have

* British Medical Journal, 1896, ii, p. 621.

† Archives of Pediatrics, April, 1897.

opportunities for clinical and post-mortem observation in large institutions.

The Mongol type of idiot resembles the cretin more closely than any other. Telford Smith, in speaking of this form, says: "Idiots belonging to the so-called Mongol type are those who most nearly resemble the cretin, both in physical aspect and in mental character. In idiots of this type we get the stunted growth, the dull, heavy expression, with open mouth and thick lips; the slow, deliberate movement, and hoarse, guttural, and monosyllabic speech; the mental apathy, and lack of spontaneity; the sluggish circulation, and sensitiveness to cold. A thickened condition of subcutaneous tissue is often found, with dulled cutaneous sensibility. The skin is coarse and dry, the hair short and thin. First and second dentition are delayed. As far as palpation enables one to judge, the thyroid gland is subnormal in size. Pseudo-lipomata I have not found." He has tried the effect of thyroid extract with some benefit, but there is not the same remarkable change as in the cretins. I cannot altogether concur with Dr. Telford Smith's statement as to the slow, deliberate movements and mental apathy of Mongolian idiots. It was a form in which Dr. Kerlin, of Elwyn, was particularly interested, and with him I had many opportunities of seeing cases. They rather impressed me as vivacious, often very sprightly and mischievous. In no instance was there any condition of the subcutaneous tissues suggestive of myxœdema.

Deaf-mutism is a not infrequent accompaniment of sporadic cretinism. In the endemic form it is still more common.

The various forms of idiocy dependent upon faulty development of the hemispheres in fœtal life, the hydrocephalic and the microcephalic idiots and the forms of imbecility associated with the cerebral palsies of children, are readily distinguished.

(*c*) *The condition known as fœtal rickets*—achondroplasia or the chondrodystrophia fœtalis—is liable to be mistaken for cretinism. On August 4, 1886, when at Cacouna in the Province of Quebec, I was asked to see two cretins, and found them remarkable rhachitic dwarfs, belonging to this type. As instances of this condition which survive birth are rare, I will here give brief statements with reference to them, and illustrations.

The parents were healthy French Canadians. There were fourteen children in the family, the eldest twenty-seven, the youngest four. Five children had died in infancy. With the exception of the dwarfs, the children were all very healthy and well grown.

FIG. XVIII.

Fig. XVIII.—Achondroplasia foetalis. Wilhelmine C., aged 16. Case described on p. 191.

FIG. XIX.

Fig. XIX.—Achondroplasia foetalis. Alphonse C., aged 11½, brother of preceding. Case described on p. 191.

Wilhelmine C., aged sixteen years, height 86.5 cm. (34 inches). (Fig. XVIII.) The mother did not remember anything abnormal about her as a young infant. She walked when eighteen months old. The head seemed large, and the mother said that the fontanelle did not close until the sixth year. When between three and four it was noticed that she did not develop naturally, and that the joints were very large. She is bright-looking and intelligent, but somewhat full and coarse-featured. The head measured 56 cm. The teeth are well formed. She talks fluently and well, and has learned to read a little, and is beginning to write, but she is backward for a girl of her age. The most remarkable phenomenon is the condition of the joints of the long bones. The shafts are short and look thin, and the articulations are very large and irregular. The shoulders are not much affected, but the elbow-joints, the wrist-joints, and the knee and ankles are enormously enlarged. She is a little knock-kneed when she stands. The mobility in the joints is perfect.

Alphonse C., aged eleven and a half years, height 87 cm. (33½ inches). (Fig. XIX.) The mother did not notice anything special about him except that he was late in walking, and the anterior fontanelle did not close until between the third and fourth years. He did not seem to grow much after the fourth year. He presents an identical picture to that of his sister. His head is large, but well formed. He is very intelligent-looking and bright, and is good-tempered. The articulations are extraordinarily large, and contrast with the smallness and shortness of the shafts of the bones. He is somewhat pigeon-breasted, and when he stands is knock-kneed.

The trunk and head in both these children look almost of natural size, but the shortness of the legs, and particularly the shortness of the shafts of the long bones is very striking. The thyroid gland was not enlarged in either case. I recognized that the cases were not cretins, and labelled them as rhachitic dwarfs, but it was some years later that I learned the true nature of the affection, namely, the chondrodystrophia fœtalis.

The relation of this remarkable condition to cretinism is very carefully discussed by Kauffmann,* and more recently by Bircher,† to whose papers the reader is referred. John Thomson, in the *Edinburgh Medical Journal* for 1893, gives excellent illustrations of the adult form.‡ The thyroid is not usually involved, though it has been found absent in a fœtus which presented this condition (Bowlby).§ The intelligence is not especially disturbed, the facial

* Untersuchungen ueber die Sogenannte Fœtale Rachitis (Chondrodystrophia Fœtalis). Berlin, 1892.

† Lubarsch und Ostertag, Ergebnisse, Abt. i, 1896.

‡ They are reproduced in Gould and Pyle's "Anomalies," etc.

§ Pathological Society Transactions, 1884.

and cranial characters are not those of cretinism, and myxœdema is not present. The most characteristic feature is the dwarfing, with remarkable shortness of the limbs (micromelia), owing to disturbance of the growth of the shafts of the long bones, and with, in most cases, enormous enlargement of the articulations, due to a hyperplasia of the cartilaginous ends of the bones. Bircher concludes that the condition is quite independent of the state of the thyroid gland. He is in error, however, when he states that the cases of sporadic cretinism described by Cushing and Fagge belong to this group.

(*d*) And lastly, the condition of *infantilism* may be briefly spoken of as in some instances dependent upon disturbed function of the thyroid, and there may be a possibility of confounding the cases with slight grades of cretinism.

Infantilism is a "morphological syndrome characterized by the preservation in the adult of the exterior form of infancy with the non-appearance of the secondary sexual characters." Lamy, in an analysis of Meige's extensive article in *l'Anthropologie* for 1895, gives the following description: "Face arrondie, joufflue, lèvres saillantes et charnues, nez peu développé, visage glabre, peau fine et de couleur claire, cheveux fins, sourcils et cils peu fournis. Torse allongé, cylindrique. Ventre un peu proéminent. Membres potelés, effilés de la racine aux extrémites. Une couche adipeuse d'une assex grande épaisseur enveloppant tout le corps et masquant les reliefs osseux et musculaires. Organes génitaux rudimentaires. Absence de poils au pubis et aux aisselles. Voix grêle et aiguë. Larynx peu saillant. Corps thyroïde généralement petit."

Occasionally the subjects of infantilism display opposite sexual characteristics—femininism not only in bodily conformations, but in mental attributes. Apart from hereditary syphilis, in which the condition is not uncommon,* infantilism seems rare in this country. It is occasionally seen combined with great obesity. More frequently it is an accompaniment of metal defects in imbeciles and idiots. The onset of puberty, with the development of the secondary sexual characters, is delayed for years after the normal age. The sporadic cretin often presents the characters of infantilism even when above thirty (see photograph of Dr. Sinkler's case), but there are rare instances of infantilism, properly so-called, complicated with myxœdematous features, due to loss of function of the thyroid, and such cases might be relieved by appropriate treatment.

* See Fournier's excellent description in "Les Affections Parasyphilitiques," 1894.

IV. THE PATHOLOGY OF SPORADIC CRETINISM.

There are three groups of cases, as noted by Dr. W. Rushton Parker:

(*a*) *With absence of the gland.* The gland has not developed in fœtal life, or become completely wasted, so that at autopsy no trace of it is found. The child may be born a cretin, which is excessively rare. In a considerable number of the reports on sporadic cretinism the thyroid is stated to be absent, but it is almost impossible to judge by palpation if the gland is very small. In one of Hilton Fagge's cases the gland was thought to be absent, but post-mortem there was a thyroid gland of some size, with tumor. Dr. Friend, of Milwaukee, has kindly sent me the full report of a case in which the autopsy showed the thyroid gland to be absent:

Hattie G., female, aged sixteen years and one month. Length of time thyroid tabloids given (Burroughs & Welcome) one year and ten months. During this time she grew from 76.5 cm. to 105 cm. Anterior fontanelle closed within six months after treatment was begun. At the end of seven months seventeen teeth of the second dentition appeared. Within the first two months the myxœdema began to disappear, and within six months was lost, the hair of the head becoming of a finer grade and very thick at the same time. The mental condition improved considerably, and as manifested by the action of the special senses, namely, hearing, sight, taste, touch, and in a slight degree, speech, the first by recognition of the voices of the nurses; the second by the attention given to the children at play in the wards and to pictures in books; the third by the refusal of certain foods and a preference for certain kinds; the fourth by a desire to grasp firm substances with the hands, so as to lift herself; the fifth by the formation and expression of two distinct words—la, da. With the augmented mental association, motor improvement was also observed. She began to sit up, and by grasping the back of a chair or bed-post, she could also hold herself standing. These associations were indicated within one and a half years of treatment. The tongue ceased protruding within six months after treatment was begun, and the salivary dribbling ceased immediately after the roots of the teeth of the first dentition were pulled and those of the second dentition appeared. The latter appeared within two weeks after the first were withdrawn. As is indicated by the photograph, Fig XI, the loss of the protruding abdomen was distinct and progressive. The blood-count never rose higher than 3,500,000 red corpuscles, and only a relative increase of lymphocytes. The urine showed no changes worthy of special note. The treatment was continued almost to the date of her death.

In reference to her death, Dr. Friend writes:

"The only cause of death manifested was two drachms of bloody fluid in the lateral and fourth ventricles of the brain. I could not discover from whence the blood came, although I examined all the blood-vessels carefully in the lateral ventricles and about the fourth. They were probably capillary diapedesis. I found all of the veins surcharged with blood, and the dura, extending about one-half inch on both sides of the longitudinal sinus, was of a deep red color. From the symptoms, especially indicated by the sudden onset of fever, I am inclined to think that the ptomaïnes in the extract of the gland may have produced a poisoning. This is, however, difficult to demonstrate. All other organs show a negative condition. The thyroid gland was absent. The thymus was very large and weighed 64 grammes. The pituitary gland was very small and weighed 0.2 grammes. Microscopically all organs showed an excess of connective tissue. In the posterior wall of the bladder I found imbedded a concretion about the size of a dime."

In reply to a question about details as to the presence or absence of the thyroid gland, Dr. Friend writes that a most careful dissection was made, and there was not even a trace of fibrous tissue as indicating the locality of the gland.

Curling first described the absence of the thyroid in cretinism in the two cases which he reported in 1850.*

Bramwell,† in a review of the literature in 1892, found ten autopsies, in which, in nine cases in which the condition was noted, the gland was absent. Fletcher Beach states that of 116 cases collected from the literature, there were sixteen autopsies, in fourteen of which the gland was absent, while in two goître existed.

(*b*) *With atrophy of the gland.* This is a very important group, to which Fagge appears to have been the first to call attention. He gives the case of "a girl, who was stated by her relations to have been perfectly healthy until she was eight years old, when she fell ill with what was supposed to be a second attack of measles, and kept her bed for a fortnight. After her recovery her physical development underwent a remarkable change. Her features were previously well formed; they now acquired the cretinous configuration. Her hair, once black and abundant, became light-colored, dry, crisp, and very scanty. She ceased to grow; at the age of sixteen and three-quarter years she was only four feet one inch in height."‡ He suggests that the febrile illness led to atrophy of the organ, and

* Transactions of the Royal Medical and Chirurgical Society, 1850, vol. xxxiii.

† Atlas of Clinical Medicine, vol. i.

‡ Fagge: Practice of Medicine, vol. i, p. 772.

2 to 3 years.

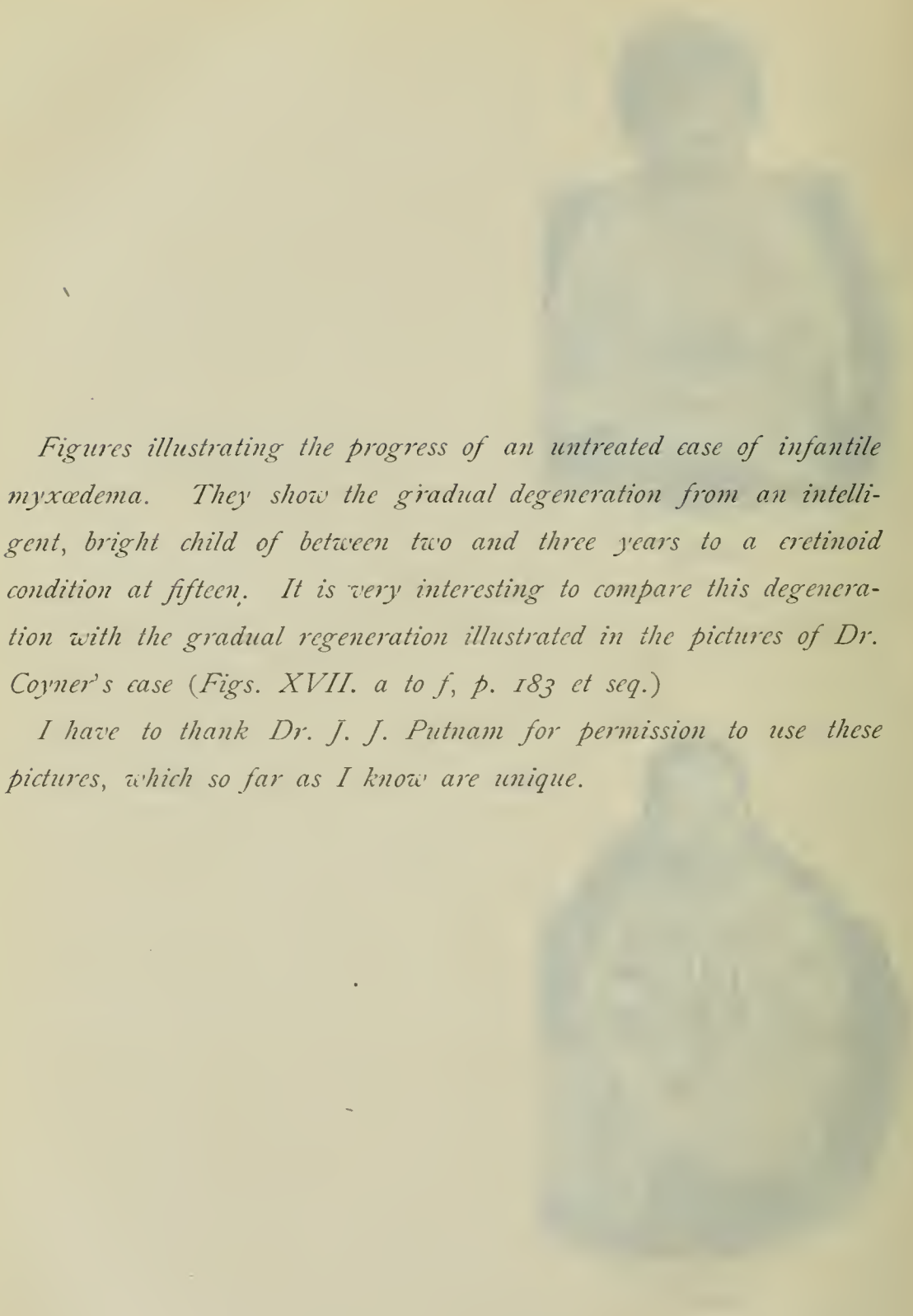
2 to 3 years.

7 years.

15 years.

15 years.

15 years.



Figures illustrating the progress of an untreated case of infantile myxœdema. They show the gradual degeneration from an intelligent, bright child of between two and three years to a cretinoid condition at fifteen. It is very interesting to compare this degeneration with the gradual regeneration illustrated in the pictures of Dr. Coyner's case (Figs. XVII. a to f, p. 183 et seq.)

I have to thank Dr. J. J. Putnam for permission to use these pictures, which so far as I know are unique.

that this was the cause of the supervention of the cretinous state. In Case II. in my first series, the condition seemed to follow an attack of enteritis. Ashby and Wright* give the history of a case said to have been well until an attack of enteric fever at seven years of age.†

It is interesting to compare these cases with the remarkable instance of operative myxœdema reported by Bruns to the Myxœdema Committee of the Clinical Society.‡ The patient at the time of operation was ten years old. Eighteen years after he had become "a dwarfy cretin." He had not grown since the removal of the thyroid, the expression was that of an idiot, there was characteristic myxœdema, with a mental apathy amounting almost to imbecility.

The determination of the atrophy of the gland during life is very uncertain, as pointed out by Fagge. No trace of the gland may be felt, and yet post-mortem a well-marked, perhaps somewhat wasted, organ is found. In the recorded autopsies in sporadic cretinism atrophy has not, so far as I can gather, been hitherto found.

Through the kindness of the officers of the Indiana School for Feeble-minded Children at Fort Wayne, I am enabled to report upon a fatal case in which there was extreme atrophy of the gland. The patient, Louise S. (Case VI. of the series), aged fourteen years, born in America, parents not related; no goître in the family; nationality German. Height, 110.5 cm.; circumference of head, 56 cm.; from occiput to root of nose, 33 cm.; from external meatus to external meatus, 26.7 cm.; circumference of neck, 28 cm. The skin is very loose and flabby, elastic and soft, very abundant. She is a deaf-mute, but appears intelligent. There is no curvature. The thorax is 57.3 cm.; abdomen, 68.6 cm. The limbs seem a little enlarged about the epiphyses. There is no goître. Dr. Delia Howe has sent a subsequent note that she had no treatment until September, 1895. She was then given the thyroid extract, three grains three times a day. She improved in many respects. The protruding abdomen disappeared, and she became very much brighter mentally. She became ill in March, and died of acute tuberculosis in November, 1896. At the time of her death she was

* Diseases of Children, second edition, p. 479.

† In the British Medical Journal, May 29th, 1897, Dr. Parker has collected ten cases of this kind, in which atrophy of the gland occurred in early childhood, either spontaneously, or following some fever. The clinical condition is spoken of as juvenile myxœdema.

‡ Clinical Society Transactions, supplement to vol. xxi.

seventeen years old, and her height was 127 cm. The thyroid gland weighed 4 grammes. The normal weight of the organ is from fifteen to twenty grammes.

I am indebted to Dr. Barker, the Associate Professor of Anatomy in Johns Hopkins University, for a careful description of the condition of the gland, which is of special value, since, so far as I can learn, there has been no histological description of the thyroid in sporadic cretinism.

The tissue was hardened in formalin and afterwards in alcohol and embedded in celloidin. Sections were stained in hæmatoxylin and eosin; in Mayer's hæmalaun, followed by eosin or by van Gieson's stain; in acid fuchsin, followed by picric-acid-water and picric-acid-alcohol; and in polychrome methylene-blue and neutral orcein.

To the naked eye a very marked increase in the connective tissue separating the lobules of the gland can be made out and, with low magnification (8—15 diameters), connective tissue can be seen entering the individual lobules and separating the acini from one another. The individual acini are seen to be almost solid; with this power no large lumina being visible except here and there where a single cyst-like dilatation filled with colloid can be made out. With higher powers the marked atrophy of the gland and the certain remarkable transformations in the epithelium of the acini become visible. In the specimens stained with hæmatoxylin and eosin, the majority of the acini in the individual lobules are found to possess very narrow lumina, often encroached upon by papillary projections inside them or partially filled up with proliferated and desquamated cells from the walls. In many acini only masses of cells are to be made out, those of the two sides coming in contact with one another, no distinct lumen being visible. The character of the cells lining the acini deviates much from the normal; indeed, one looking at the majority of the follicles under the high power, and not knowing the origin of the specimen, would scarcely be able to recognize the tissue as thyroid. The cell bodies vary a great deal in size, from small cells about equal in dimensions to those of the normal thyroid gland to large flat structures many times the size of the former, actual giant shells. The individual cells in a single follicle are not all of the same size; in the majority of follicles numerous transition stages exist between the small cells and the cells of greatest dimensions. The cells show no constant arrangement in the wall of the follicle, but appear

to be mixed up quite irregularly, very small cells being sometimes immediately adjacent to giant cells, at other times being separated from them by cells intermediate in size.

The borders of the cells are for the most part difficult to make out with ordinary powers, though the outlines of the giant cells with jagged margins can be seen. With oil-immersion lenses, however, the borders of nearly all the cells can be easily defined. The protoplasm of the cells lining the acini in specimens stained in hæmalaun and eosin stains of a reddish brown and brownish pink color, a tint quite different from that assumed by the connective tissue, which takes the simple eosin stain. The protoplasm of the individual cells varies somewhat in appearance, though in the majority of them it has a dull opaque, almost homogeneous look. With very high powers, and cutting off the light, minute white dots of variable size can be made out. In some cells a reticulum-like structure is visible, consisting either of delicate fibrils, or possibly of granules arranged in rows. The meshes are filled with a paler, more refractive substance. Occasionally, a single cell presents a distinctly vacuolated appearance. The cells are all, or nearly all, higher than normal thyroid cells, although a few alveoli lined by flat or low epithelium were met with.

The nuclei of the cells lining the acini show marked alterations. By far the majority of them are larger than normal, many of them being huge, bladder-like nuclei. These are more frequently seen in the largest cells. The nuclei exhibit in various degrees the phenomena which have been classed under the term "karyorrhexis." There appears to be an increase in the nuclear juice and a displacement, in many of the nuclei, of the chromatin-substance from its normal situation. In some nuclei a peripheral disposition of the chromatin is visible, the central parts being more or less decolorized (Kernwandhyperchromatose of the Germans). In such nuclei it is possible to make out not infrequently the remains of the nuclear framework and of nucleoli, in the shape of pale strands and spherical masses, deprived of their color. In other nuclei clumps and false bands of chromatic substance are present throughout the nuclear mass (Gerüsthyperchromatose of the Germans). While many of the nuclei are on the whole paler than normal, more of them stain more intensely than those of the normal thyroid gland; some of the large, bladder-like nuclei stain feebly, others intensely. The intense stain occurs especially in those of them which show very jagged and irregular borders (Verklumpte Kerne of de Cou-

lon). Some of the largest nuclei give one the impression of loose-walled bags without tonicity. At different parts of the surface the nuclear wall is collapsed and depressed, the depressions being filled up by masses of cell protoplasm. No mitoses are visible. A number of nuclei, as a rule deeply staining ones, show projecting buds of nuclear substance which extend from the general mass of the nucleus into the cytoplasmic substance. These are often constricted by a narrow neck and, in a few instances, masses of nucleus appear to be actually separated from the main body, representing a form of nuclear fragmentation. This appearance, however, was met with only rarely.

As a rule, each cell contains a single nucleus, though in a few instances two nuclei are present and in one cell no less than six spherical, rather deeply staining, nuclei were found in one large cell body. These nuclei appeared to be entirely separate from one another and lay in different planes in the cytoplasm.

The lumina of the acini, as has been said, vary much in size. Some of the alveoli really possess no lumina at all; in others only a very small central opening is to be made out, while in others there are larger lumina, a few of the size of normal thyroid alveoli. Extremely few of these acini contain any colloid; the majority are either entirely empty or show inside them only desquamated cells from the alveolar walls. A very few cysts are present, filled with colloid substance. These cysts are of the size of from three to six normal thyroid alveoli and are lined by flattened thyroid epithelium, which otherwise appears to have undergone very little change. Some of these have evidently been formed by the fusion of several acini, for the broken walls of separation can be seen projecting in from their margins. They are almost completely filled with colloid, which is not markedly retracted at the borders. The colloid stains of a rose red color in eosin specimens. No accumulation of leucocytes could be made out within any of the acini or colloid cysts.

The stroma, which is very much increased in amount, consists of firm, white fibrous connective tissue. As a rule, this is not very cellular; in the parts of the gland which appear to be undergoing the most rapid atrophy, however, the nuclei are more numerous. In these regions one sees considerable numbers of blood vessels undergoing obliteration and surrounded by concentrically arranged, young connective tissue cells. Near them are groups of acini in various stages of atrophy. Some of these are reduced so much in size that they consist simply of groups of two or three epithelial cells

surrounded by connective tissue; indeed, in a number of instances, single cells, undoubtedly thyroid epithelium, are to be made out lying isolated in connective tissue masses. These are evidently also the remains of acini.

No very remarkable alterations are to be made out in the blood vessels. The blood is fairly well preserved and the capillaries projecting into the larger acini are filled with red blood corpuscles. A large number of nerves, both medullated and non-medullated, are present in the section, usually near large blood vessels, but no pathological alterations are to be made out in them.

The specimens stained by van Gieson's method, with and without preliminary nuclear staining with hæmalaun, yield excellent pictures, especially for a comparison of the relative amounts of parenchyma and stroma, inasmuch as the epithelial cells are stained bright yellow and the connective tissue stroma takes the acid fuchsin. By means of this stain, spherical masses can be seen within the protoplasm of some of the cells lining the acini. Whether or not these masses are colloid or an allied substance, could not be determined. At any rate, they stain of a yellow color quite like the rest of the protoplasm. The colloid in the cysts mentioned varies in its behavior toward van Gieson's stain. In some of the few cysts present it is of a bright yellow tint; in others it stains of a reddish brown color and is then more refractive. In the connective tissue one or two spaces filled with refractive colloid matter were found. These probably represent lymph vessels, but there is certainly no great amount of colloid inside the lymph spaces, nor is any colloid to be seen within the blood vessels.

Specimens stained with acid fuchsin and differentiated in picric-acid-water and picric-acid-alcohol afforded results essentially the same as those obtained by van Gieson's method, with the exception that, with this procedure, a certain number of the red corpuscles showed a greater tenacity than others for the acid fuchsin. These corpuscles remained stained of a bright red color, after all the rest had lost it and were stained yellow in the picric acid.

Sections treated with polychrome methylene-blue and neutral orcein are of service for studying the cells and the stroma. The nuclei stain blue; the protoplasm assumes a violet tint, while the collagen of the connective tissue fibres stains reddish brown in the orcein. With this method the irregular borders of the epithelial cells in many of the acini were particularly striking; the cells looked ragged at the edges and gave the impression as though they

were losing parts of their substance at the periphery. The vacuolization of the cells is very apparent in these sections also. The cytoplasm of some of the larger cells containing degenerated nuclei possesses an especial affinity for the orcein, staining of a reddish brown color.

A review of the bibliography shows that only eight cases have been reported in which the thyroid has been described in cretins; namely, three cases by Hanau, one by Langhans and four by de Coulon. While there are minor differences, the process in all cases thus far described is essentially the same. The findings in this case are in the main confirmatory of those which have previously been made. De Coulon's descriptions* are particularly full, and the illustrations accompanying his article, especially his figures 1, 2 and 3, agree very closely with what is to be seen in the specimens here described. It is rare, however, to find acini with as much colloid inside them as he shows in his first two figures. That, in addition to the evidence afforded by the size of the gland and the marked increase of connective tissue in it, the cellular and nuclear changes are atrophic and degenerative in nature, there can be but little doubt. The nuclear changes especially are those which are now generally recognized as characteristic of degenerative processes. They correspond in many respects to some of the lesions described by Oertel in human diphtheria and by Flexner in experimental poisoning of animals with diphtheria toxines. Schmaus and Albrecht believe such nuclear appearances to be evidences of degeneration. The degree of retrogression in the thyroid gland of this case is one of the most marked which has yet been reported, though apparently in De Coulon's cretin, Santschi, the atrophic process had gone even further.

(*c*) *Sporadic cretinism with goître.* Of the sixty cases collected in this country, seven had goître. Herein lies a very striking difference between the sporadic and the endemic cretinism. In the latter the percentage of goître in some statistics has been as high as sixty (Knapp). In Fletcher Beach's collected statistics of one hundred and sixteen sporadic cretins in different countries, the thyroid is noted as "not felt" in seventy-three; "felt" in eleven, and enlarged in seven cases. He states that of sixteen post-mortems of which he has been able to find an account, the thyroid gland was absent in fourteen cases, and there was bronchocele in two.

Through the kindness of Dr. Darey, of Northwood, Iowa, and of Dr. Kessel, of Cresco, Iowa, I am enabled to report upon and show

* Virchow's Archiv., 1897.

the photographs of two remarkable goîtrous cretins.* The father's sister had goïtre. There were five children; one died at the age of eight months, of diphtheria; one is alive and well, and has no goître, and three have had goître; one died at the age of eight years, following an operation on the goître. In the two whose photographs are given here the goîtres made their appearance when they were quite young infants. The notes of the cases have been given (XXXIV and XXXV). (Figs. X and XI.)

V. THE RELATIONS OF SPORADIC TO ENDEMIC CRETINISM.

When the "cretinoid state," to use Gull's expression, whether developing spontaneously or following thyroidectomy, became recognized as a direct result of the loss of the function of the thyroid gland, it was a simple matter to suggest that true cretinism, both sporadic and endemic, had the same origin. The generic term cretinism may indeed be used to cover these four allied states—endemic, sporadic, idiopathic of adults (myxœdema), and operative —following total excision of the gland. One and the same pathological basis exists in the entire group—viz., loss or perversion of the function of the thyroid; the anatomical basis is varied—total absence, atrophy or goître. Kocher,† in his masterly presentation of the subject, takes this wide ground. Without exception, so far as I know, recent writers have assumed this position, but quite recently this relationship has been questioned by Bircher, a well-known student of endemic cretinism, in an excellent section on the "Thyroid Gland," in Vol. I. of Lubarsch and Ostertag's *Ergebnisse*, etc., 1896. He concludes "that the cretinoid degeneration is in no way connected with disturbance in the function of the thyroid gland." He bases this opinion upon the persistence of the thyroid, cystic, and degenerated, it is true, in a large proportion of cases. In twenty cases, fifteen had goître, four normal thyroid glands, and in one only it could not be felt. In three cases in which he had extirpated the thyroid in cretins and in the non-degenerated parts he had found normal thyroid tissue. Moreover, a cretin from whom he removed the cystic goître became myxœ-

* They remind one of Shakespeare's description in the "Tempest" of the

> "Mountaineers
> Dew-lapp'd like bulls, whose throats had hanging at 'em
> Wallets of flesh."

† Zur Verhüting des Cretinismus und Cretinoid Zustände nach neuen Forschungen. Zeitschrift f. Chirurgie, Bd. xxiv, 1892.

dematous, and was temporarily cured by the implanting of a gland; but, as Hanau and Ewald both remark, this is no evidence that the thyroid has nothing to do with cretinism. It would be very much the same as the development of uræmia in a case of chronic nephritis after bilateral nephrotomy.

Both Curling and Fagge believed the conditions which they described to be identical with endemic cretinism. They further have the great merit of recognizing the loss of function of the thyroid as the probable essential factor in the disease. Curling's title is in itself suggestive: "Two cases of absence of the thyroid body, and symmetrical swellings of the fat tissue of the neck, connected with defective cerebral development." In seeking an explanation he speaks of "the absence of those changes which result from the action of the thyroid, or on some imperfection in the assimilating processes consequent on the want of this gland; and the facts here detailed may not be without significance in directing the researches of future inquirers into the use of this body." Fagge held that the presence of the thyroid gland was "prctective against the occurrence of cretinism." A similar opinion had been expressed about endemic cretinism in 1830 by Troxler (Kocher).

We may ask in the first place, are there any essential differences between the sporadic and endemic forms of cretinism? A single definition covers both conditions—*a chronic affection characterized by disturbance of the growth of the skeleton and soft parts, a remarkable retardation of development, an extraordinary disproportion between the different parts of the body, a retention of the infantile state, with a corresponding lack of mental progress.* One has only to compare the picture given of cretins in Switzerland with those of the sporadic form, both in England and this country, to see that the two states, so far as external characters go, are identical. The differences between the two forms are as follows:

1. The endemic variety develops under local conditions as yet unknown, associated with a peculiar poison of doubtful nature. Bircher states that "the cretinoid degeneration is a chronic infectious disease, the organic miasm of which is associated with certain marine deposits of the earth's surface, and which gains access to the body through the drinking water." It is only of late years that any light has been thrown upon the intimate relation of goître and cretinism. I have already referred to the opinions of Troxler, Curling, and Fagge, and almost all writers on the endemic form agree with the statement of Morel, that goître is the first step on

the road leading to cretinism. It is possible, however, that changes other than those which lead to goître may be effective; anything which causes loss of function of the gland.

2. The differences in the changes in the bony skeleton. In the endemic cretin a premature ossification of the spheno-basilar bone has been described, and the fontanelles close early. How far these are constant characters remains to be demonstrated. In the sporadic form the fontanelles often remain open for a long period, even until after the tenth year, and there is a greater retardation in the development of the long bones.

3. The endemic cretin is said not to show the same myxœdematous characters as the sporadic cretin, but the accounts vary in different authors; and the description of the cutaneous condition given by Kocher (whose experience with cretinism has been very large) fits that of the sporadic cretin exactly. Other minor differences are mentioned, such as the shorter life of the sporadic cretin; Ewald,* indeed, states that he knows of no instance in which life has been prolonged beyond the thirtieth year, but of the cases which we have collected there were seven beyond the thirtieth year. Another point is the less frequent presence of goître. The percentage of goître in endemic cretins has been noted as high as sixty; in the Sardinian Commission there were 3912 instances of goître in 5923 cases. In the collected series of sixty cases there were only seven with goître. The two cases with goître, figures X and XI, are good examples of goîtrous cretins occurring in a family in which goître was prevalent.

4. Bircher states that the thyroid extract has no influence upon endemic cretins, a fact which he claims illustrates the independence of loss of thyroid function; but I cannot gather that he, or, indeed, anybody else has systematically tried the thyroid treatment upon young cases. There is some positive evidence. Kræplin† (who holds that in endemic cretinism disease of the thyroid is the first link in the chain, and that changes in the skin, retardation of growth, and dementia result directly from loss of function of the thyroid) speaks most hopefully of arresting the disease by thyroid feeding if begun early. He adds that even in long-standing cases it has been possible by the thyroidin to wholly reduce the swelling of the skin, and he has seen the menstrual functions restored. The psychical features were not much improved.

* Nothnagel's Specielle Pathologie und Thérapie, Bd. xxii, the most recent account of cretinism and allied states.

† Psychiatrie, fifth edition, 1896.

Prof. Gaule, of Zurich, writes me that he is informed by Kocher that all the cases that are brought to the hospital are treated with the thyroid extract.

Prof. Sahli, of Berne, writes that "so far as I know, the observations on operative myxœdema have been confirmed by the thyroid treatment of young cretins." The question is one deserving of the most careful study in the goître and cretin districts of Europe.

The minor differences between endemic and sporadic cretinism, many of which are still doubtful, cannot for a moment be set against the similarity of the two conditions in almost all points save the local (telluric) influences in the causation of the former; and there only remains the question of the state of the thyroid gland. It is remarkable that in endemic cretinism the observations should be so scanty. Hanau* reports three cases, in all of which the thyroid glands showed alterations, being smaller, and in one there was a cyst. The connective tissue was abundant, the alveoli smaller, and in only a few was there the normal colloid. Langhans,† in one case, found the gland enlarged, and made up of large alveoli, many of which were empty and only a few filled with refractive colloid. De Coulon,‡ working in Berne, has examined the thyroid gland in four cretins, and in one cretin of bodily form, but good mental development, and after a most thorough histological study, concludes "that the thyroid had not completely degenerated, but the tissue showed changes which indicated that its function was impaired, or at least reduced to a very low ebb. The smallness of the alveoli, their disappearance in consequence of the relative increase in the connective tissue, the absence of colloid in the majority of the alveoli, and in almost all the lymph vessels, so also the condition of the epithelium and the nuclei . . . speak in favor of this view." Also the condition of the existing colloid and its reactions suggested, he thought, important chemical changes of a degenerative character.

In the atrophied gland of Case VI. the lesions were identical with those found in one of de Coulon's cases, which still further strengthens the position of those who hold the essential unity of the process. In neither form is the state of the thyroid gland always the same; loss or serious perversion of function is the important factor, and this may follow absence, atrophy, or hypertrophy. There is no fixed stamp or type of cretin; the range is from a mere

* Transactions of the Berlin International Congress.

† Virchow's Archiv., Bd. cxxviii.

‡ Virchow's Archiv., Bd. cxlvii.

mass of humanity without a ray of intelligence, to the high-grade cretin with but slight bodily and still slighter mental changes; and it is only reasonable to believe that to these grades are correlated varying degrees of thyroid degeneration. Bircher lays great stress upon the presence of normal-looking tissue in the glands which he excised from cretins, but gives no statement of any histological study; nor is the development of myxœdema in one of these cases, and of tetany in another, inconsistent with the view that the thyroid is the seat of the essential lesion, since the activity of the gland may have been sufficient only to maintain the organism at a certain plane of cretinoid existence.

If the experimental work on the importance of the para-thyroids should be confirmed, the whole question will have to be reviewed from this standpoint.

There are, of course, gaps in our knowledge, but the evidence at present available warrants, I believe, the conclusion that the changes characteristic of cretinism, endemic as well as sporadic, result from *loss of function of the thyroid gland.*

VI. OPERATIVE MYXŒDEMA.

It is somewhat remarkable, considering the number of times thyroidectomy has been performed in this country, that operative myxœdema is so rare. In my previous paper I reported, through the kindness of Dr. McGraw of Detroit, a case which had occurred in his practice. Dr. McGraw writes to me on the date of April 9th, 1897, that this patient was placed upon thyroid extract and immediately began to improve. The myxœdema disappeared, the hair grew, and he has been able to resume his work. He has, however, to take the thyroid extract at intervals.

I have had sent me also the notes of another case by Dr. John C. Fisher, of Litten Springs, California, which is evidently a very typical and remarkable one, and has also got perfectly well. A very interesting feature in this case is that the treatment should have been begun so many years after the development of the condition.

Miss J. L. T., aged thirty-three, born in United States.

"At the age of thirteen years, in the month of July, 1873, an operation was performed to remove a swelling from the neck. This swelling had been growing rapidly for four months. The operation was successful. Six days after the operation a severe hæmorrhage began. We lived near Buffalo and some doctors came from that

city to attend me. The hæmorrhage was not stopped until thirty-six hours afterwards. After I got well and could eat, everything turned to flesh."

The doctor writes, "when I saw the case twenty years after the operation, the patient presented a typical case, as described in literature. She was evidently nearing death. Two assistants were necessary when she walked. I put her on P. D. & Co. dessicated thyroids, two grains t. i. d., increasing to five grains t. i. d. Improvement was immediate and most pronounced. Treatment begun in May. In August the lady went to the World's Fair and walked four or five miles daily without fatigue. She writes that it is necessary to take the thyroid treatment for a short time, now and then, in order to keep in good health. The patient says 'I call myself perfectly well, and my friends all consider it a wonderful cure.' "

FIG. 1.

Fig. 1.—Double congenital dislocation of the hip; showing the lordosis.

CONGENITAL DISLOCATION OF THE HIP.

BY EDWARD H. BRADFORD, M.D.

Assistant Professor of Orthopedics in Harvard University.

It is the function of the specialists to examine and report on questions lying beyond the limits of accepted facts. In this way specialization is justified furnishing outposts to the larger force marshaling the whole profession of medicine and surgery.

The subject of Congenital Dislocation of the Hip has for the past decade been under careful consideration, and as the brilliant successes that have been recently gained were largely won by two honored members of our Orthopedic Association, it may be fitting in a representative of that Association to present the subject in a triennial address before the General Congress.

It is not within the province of this paper to relate the history of the various attempts in the past to cure congenital dislocation of the hip, though this is an interesting chapter in the history of surgical progress of this century. Briefly, it may be said that the world is especially indebted to the efforts of Hoffa and Lorenz. Previous investigators accumulated facts which have served as a preparation for later successes.

In considering the subject, an accurate knowledge of the pathological anatomy, fortunately now well understood, is of importance. The etiology of the affection, however, is not known, though it is clear that true congenital dislocation is an affection of the uterine life. It would seem also that it is not a defect of development like hare lip, but like congenital club foot, a malposition of bones with the resulting structural changes of the soft parts. It is a fact that the affection is much more common in girls than in boys for some unknown reason. (Fig. 1.)

The theory that the affection is due to inter-uterine pressure will appear to be substantiated by an infant specimen published by Mr. Jackson Clark in the Transactions of the British Orthopedic Society, 1896, Vol. I, page 36, where in uterine life the thighs were apparently flexed for so long a period without extension, as to cause the firm contraction of the anterior portion of the capsule. Later extension of the limb, possible from an increase of amniotic fluid or from any cause, would, in a shallow acetabulum, cause dislocation of the hip.

PATHOLOGICAL ANATOMY.

Changes in the Capsule.—The most important of the anatomical changes to be observed are the changes in the capsule. The capsule is not ruptured, as in a traumatic dislocation, but is gradually stretched. The upward ascent of the head is increased as the child's weight increases, and the capsule is dragged with it. It becomes even at an early age much thickened, especially in its anterior surface, and the shape of the capsular cavity is changed from that of an irregular globe passing from the rim of the acetabulum to the attachment around the neck of the femur. The capsule may be described as in shape like an empty purse bag, glued to the iliac bone, the lower portion covering the acetabulum; the free portion enclosing the femoral head, and the purse neck, the part where the head of the femur left the acetabulum, stretching the adherent capsule with it.

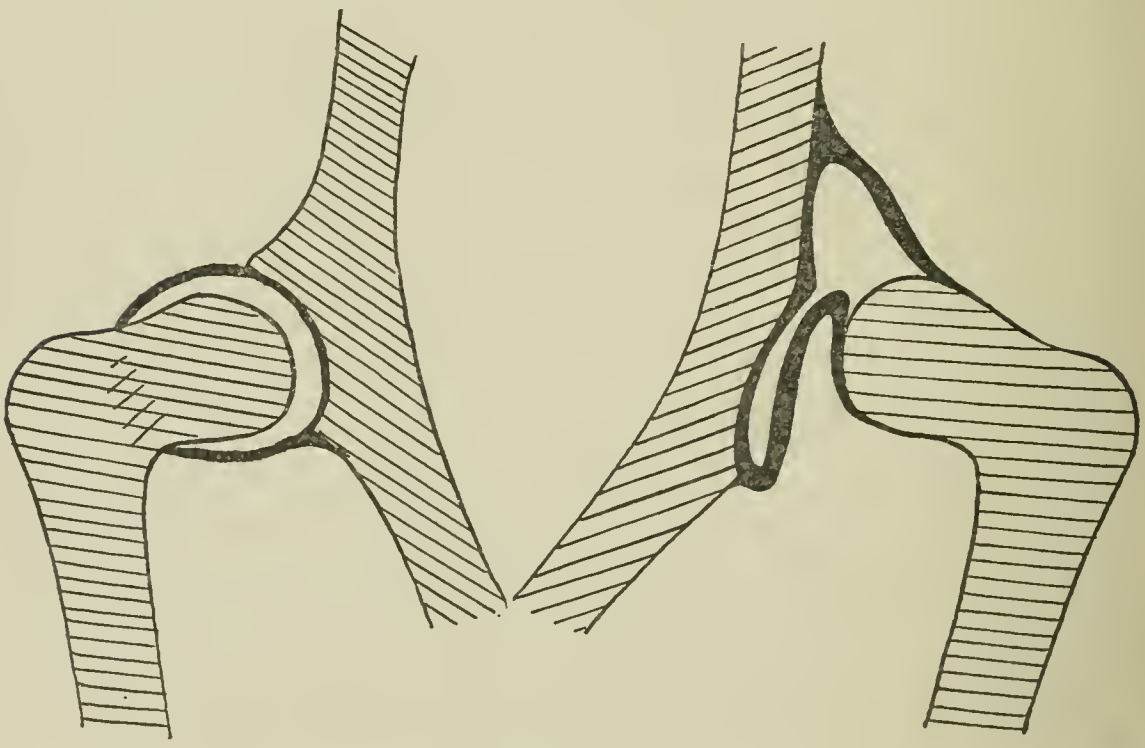


FIGURE 2.

Diagrams illustrating section of the capsule in a normal hip-joint and in a congenital dislocation of the hip.

What may be termed the neck of the capsule is attached on its iliac surface to the ileum, and this attachment may be unusually firm; that portion of the capsule covering the acetabulum becomes altered and with the changes of the synovial membrane and

stretched cotyloid ligament resembles firm, fibrous tissue filling, as well as covering the socket, so that the cavity may be obliterated.

Alteration in the Muscles.—Much discussion has taken place in regard to this important matter. The arguments and observations of Lorenz, however, may be accepted. It is not true, as has been previously claimed, that all the muscles that pass from the pelvis

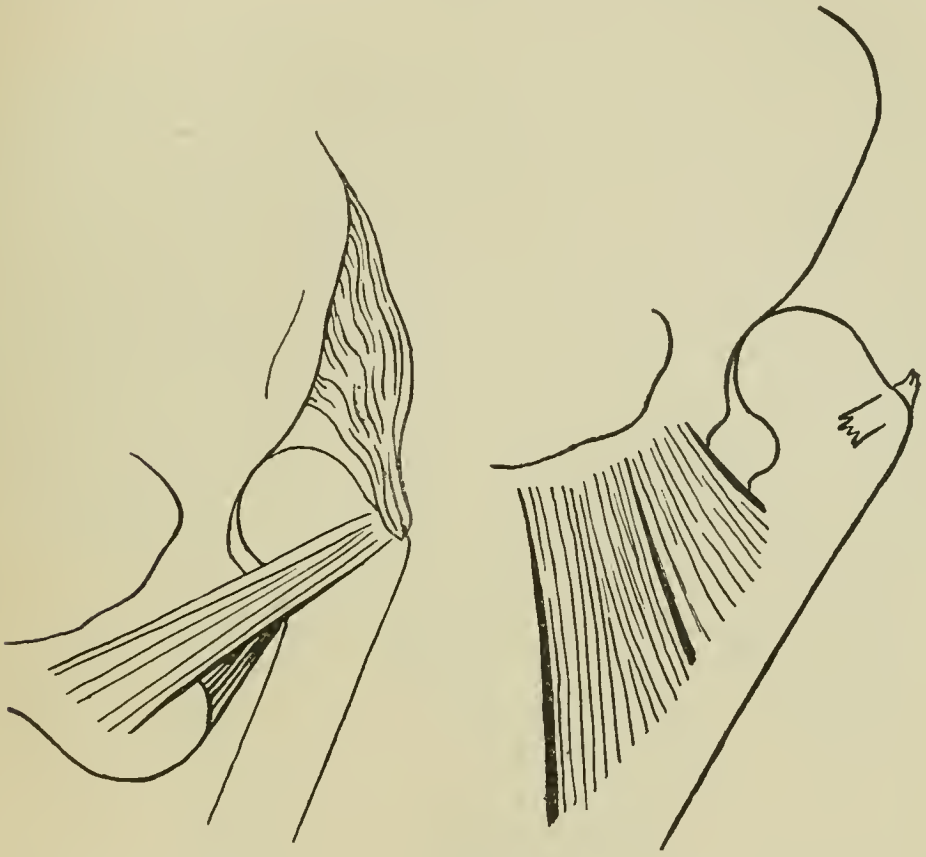


FIGURE 3.

Diagram showing pelvi-trochanter and pelvi-muscles in congenital dislocation of hip.

to the trochanter are shortened and constitute an obstacle to reduction. The glutæi are somewhat altered in size and structure from alteration of this function from the difference in direction in which they move, but are not contracted, and the group of muscles which surround the acetabulum and pass around the neck of the femur to the great trochanter, i. e., the pelvi trochanteric muscles, are lengthened. The pelvi femoral muscles, i. e., those inserted along the shaft of the femur, are, however, shortened, especially the adductors. This is also true of the pelvi crural muscle.

Alteration in the Bones.—It is due to Hoffa that it is now clear that the altered soft parts, and not an absence of the acetabulum, present

the chief difficulty in reducing a congenital dislocation. The acetabulum is altered in its shape, becoming triangular instead of oval, and may be broadened and flattened. The cartilage which normally covers the socket disappears, except at the rim, and is replaced by fibrous tissue. The formation of a new false joint with osseous socket is not seen in congenital dislocation in children; it is

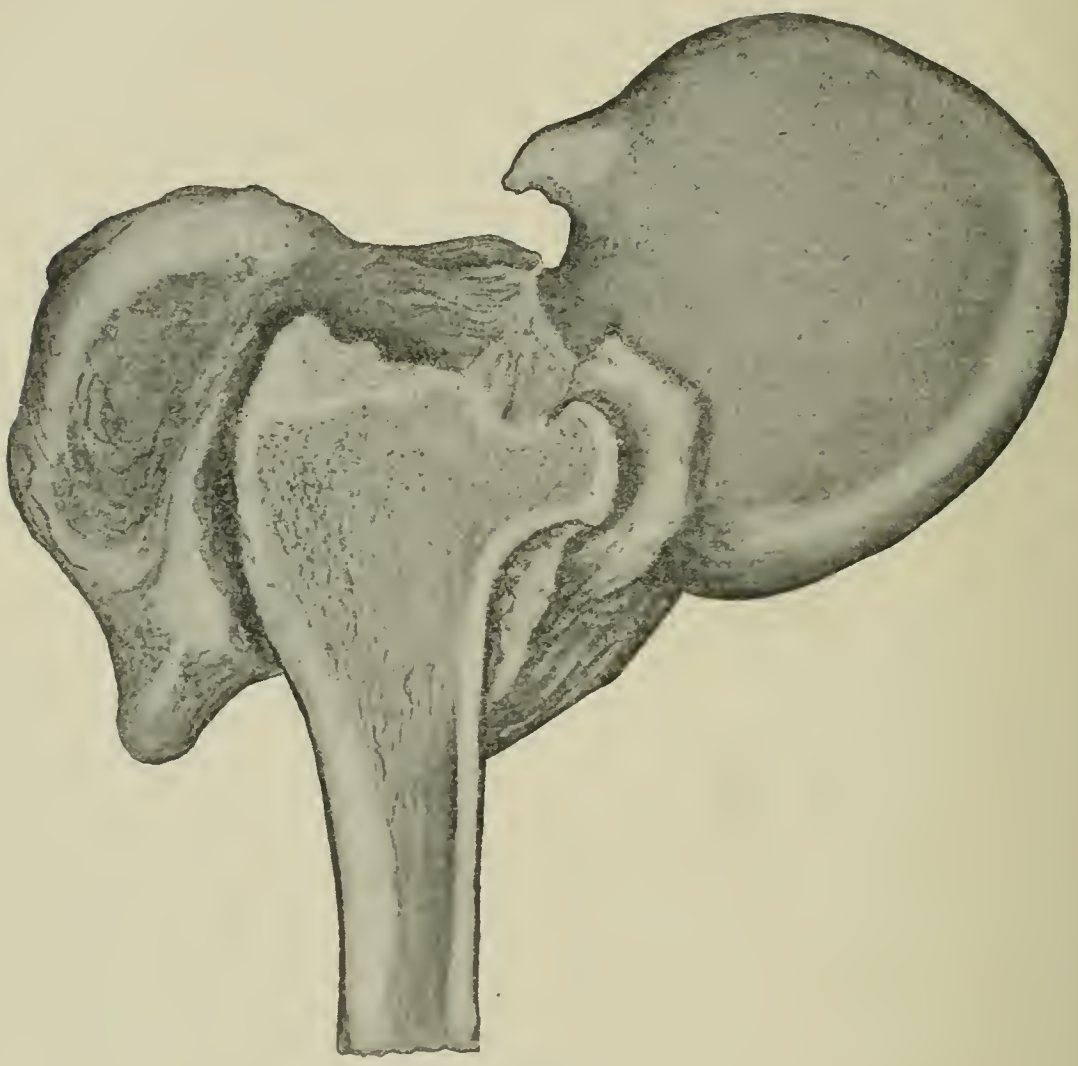


FIGURE 4.

Specimen of congenital dislocation of the hip with femur (head and neck) sawn: the acetabulum is not seen: the thickened capsule is shown. Warren Museum.

extremely rare in adults, though a depression in the surface of the ileum at the point where the head of the ileum rests is to be seen. The neck of the femur is frequently altered in two directions; the normal obliquity is lost, the neck being at right angles with the shaft. A twist in the neck is also seen. The shape of the head is

frequently altered, the round shape is changed into a pointed one and, in some instances, the head is much smaller than normal.

There are three varieties of congenital dislocation, classified according to the position of the head. They may be classified as

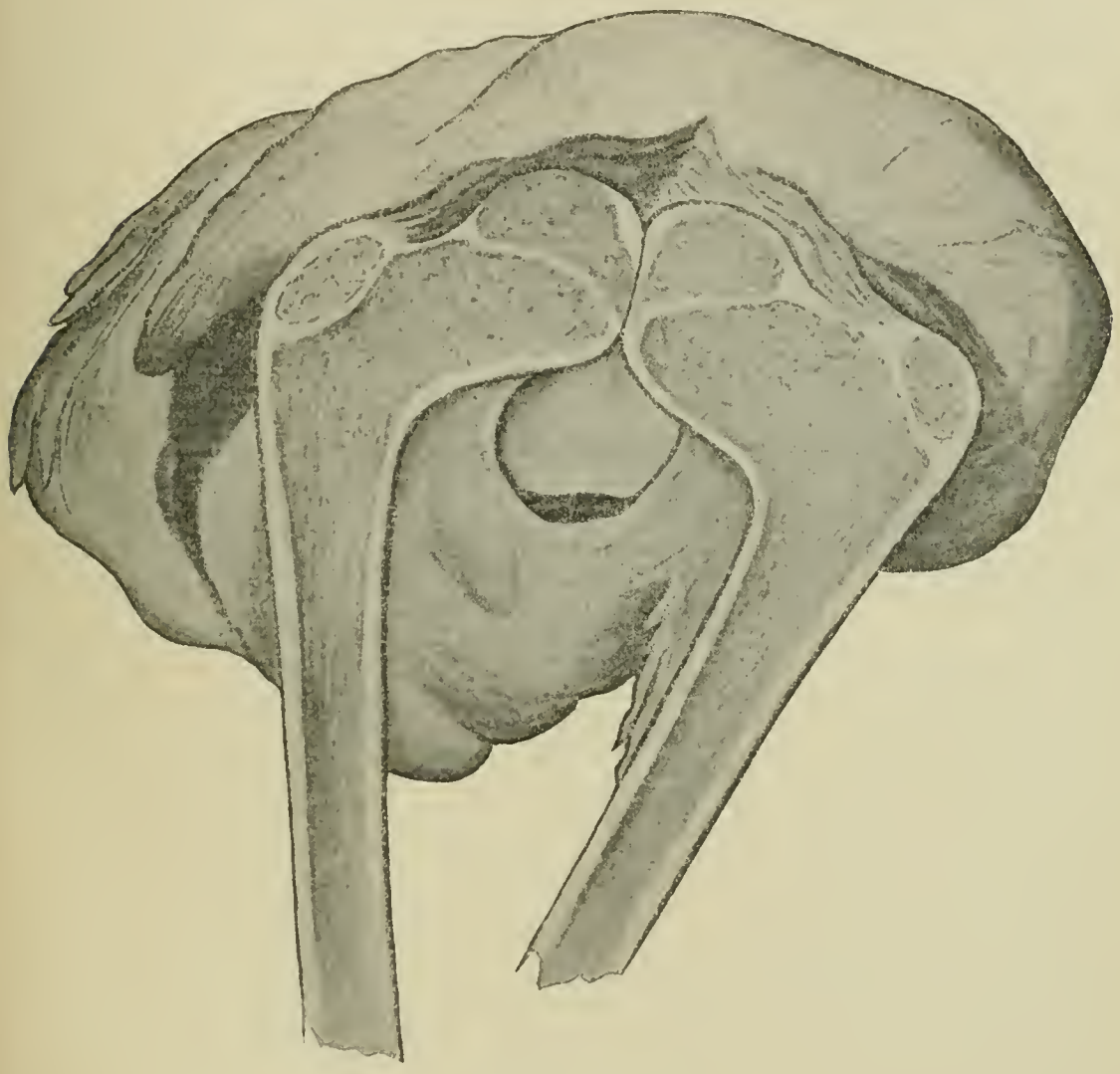


FIGURE 5.

Specimen of congenital dislocation of the hip. Femur sawn through head and shaft, turned back showing the opened capsule. The dark space is the acetabulum nearly covered by the capsule. Warren Museum.

backward, upward, and forward. In the backward, the head lies upon the dorsum of the ileum, resembling the position of the usual traumatic dislocation. In the upward dislocation, the head rests above the acetabulum; and in the forward, the head lies nearly beneath the anterior superior spine. In the latter case, the foot is drawn somewhat outwards; in the former, it is necessarily turned

in, or this would be the position if it were not for alterations in the shape of the neck.

NOTE. The anatomical changes in congenital dislocation are well illustrated by four specimens in the Warren Museum, carefully examined by Dr. E. H. Nichols, Instructor in Surgical Pathology in the Harvard Medical School. The alterations in the capsule here mentioned are demonstrated in two of the specimens in alcohol, and the twist in the neck of the femora in the two dry specimens.

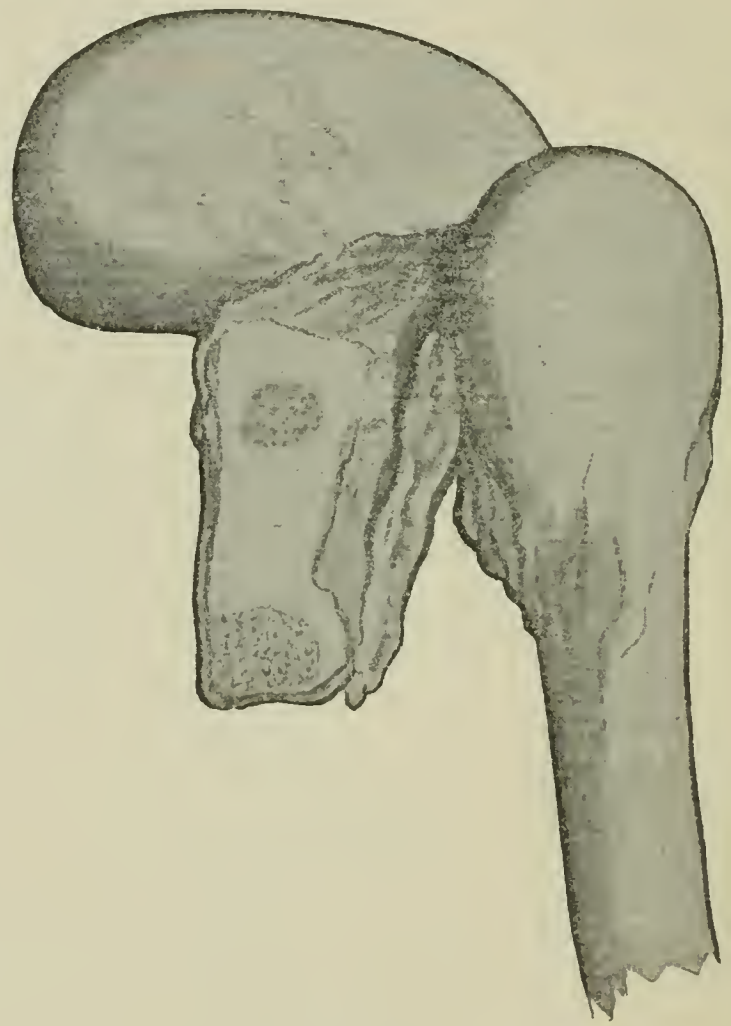


FIGURE 6.

Specimen of congenital dislocation of the hip. Section through the acetabulum showing the covering of the acetabulum by the reflected capsule and the shallow acetabulum. Warren Museum.

DIAGNOSIS.

The diagnosis of this affection is not difficult in adult cases or in large children, as the characteristic peculiarities in gait and attitude are easily seen.

The following affections may be confounded with it in smaller children, coxavara, distortion following infantile paralysis, separa-

tion of the epiphysis, deformity following early arthritis of infancy, and traumatic dislocations, and the deformities of hip disease.

In all of these affections, with the exception of the first, viz., coxavara, there should be a history of previous injury or illness; and in all, with the exception of coxavara and infantile paralysis, the freedom of motion of the femur seen in early congenital dislocation is not found.

Coxavara, or the rachitic distortion of the neck of the femur, which shortens the limb and raises the trochanter above the Nelaton line, may be confounded with congenital dislocation.

The mistake can be avoided, if the fact is borne in mind that in coxavara the head is in its normal socket, while in congenital dislocation the head is to be felt outside of the acetabulum.

Coxavara is rarely seen before five years of age, and is only very exceptionally noticed as early as three.

In small children with fat buttocks it is sometimes difficult to find with certainty the dislocated head. As Delanglade has pointed out, the diagnosis is aided by remembering that where the head of the femur is in the acetabulum, rotation takes place with the acetabulum as the center, and the neck as the radius of the arc of motion; where the head is out of the acetabulum, and the trochanter is the center of motion, the looser head describing the arc.

The affection congenital dislocation is occasionally regarded as a disease of the spine, as marked lordosis is always present, and in many instances spinal corsets have been applied, with the idea that this is the chief source of the trouble. The affection, singularly enough, causes but little anxiety in the minds of the parents, who either do not notice the difficulty or who look upon the peculiarity in gait as due to an infantile habit. The peculiar side-to-side gait of double congenital dislocation is pathognomic. When the affection is unilateral, the gait is also characteristic and has been aptly compared by Saint Germain to the gait on the free side of an organ-grinder carrying a barrel-organ. The gait is due to the patient's attempt to diminish the strain upon the ligaments sustaining the weight, and to supplant the glutæi whose function is impaired.

Fluoroscopic examination, when available, is of great value in diagnosis.

PROGNOSIS.

The disability caused by this affection in childhood is slight. The limp is noticeable, and in double congenital dislocation may be distressing. As the patient becomes older and the weight

increases, some annoyance may be caused in adolescence, but the disability is ordinarily not great until middle life or old age. In single dislocation, the disability in adults may be only an inability to engage in active occupation, accompanied by occasional attacks of severe muscular pain with muscular cramps. These attacks subside under rest, but if the patient become heavier or feeble may necessitate the use of crutches and severe disability. Where the dislocation is on the dorsum, the disability is greater than where it is anterior or above the acetabulum. Muscular patients suffer less than those with feeble muscles. In double dislocation the disability is increased.

The pelvis, though altered in shape, does not appear to be changed in such a way as to interfere with child-birth.

TREATMENT.

In congenital dislocation the weight of the trunk does not fall normally upon the lower extremities; the body may be regarded as slung to the femora by the capsule aided by certain muscles, in the same way that the carriage of the last century was slung to the truck by straps. No cure of congenital dislocation is complete until the dislocation is reduced and it is certain that the weight of the trunk is supported on the head of the femur resting in the acetabulum.

As the tissues present obstacles in the shape of thickened capsule, shortened and misplaced muscles, an altered acetabulum and a misshapen femoral head, the procedure of reduction needs force or incision to stretch or divide contraction, means to deepen the socket, besides skill in manipulation for reduction. The methods for consideration can be grouped as,—

Reduction after incision.
Reduction by forceful manipulation.
Gradual reduction by mechanical appliances.

Reduction after Incision.—Operative measures, apart from excision, were first performed by Poggi and Marjory, but it is to the credit of Hoffa that a successful method has been presented to the profession. Lorenz has improved the details both of reduction after incision and by forceful manipulation.

The patient is to be placed upon the back, with the limb abducted and rotated outward. The excision is made in a line drawn from in front of the anterior superior spine, obliquely downward and forward, crossing the femur a short distance below the top of the trochanter. The incision should be along the outer

edge of the tensor vaginæ femoris, between this and the anterior border of the gluteus medius. The incision should pass well below

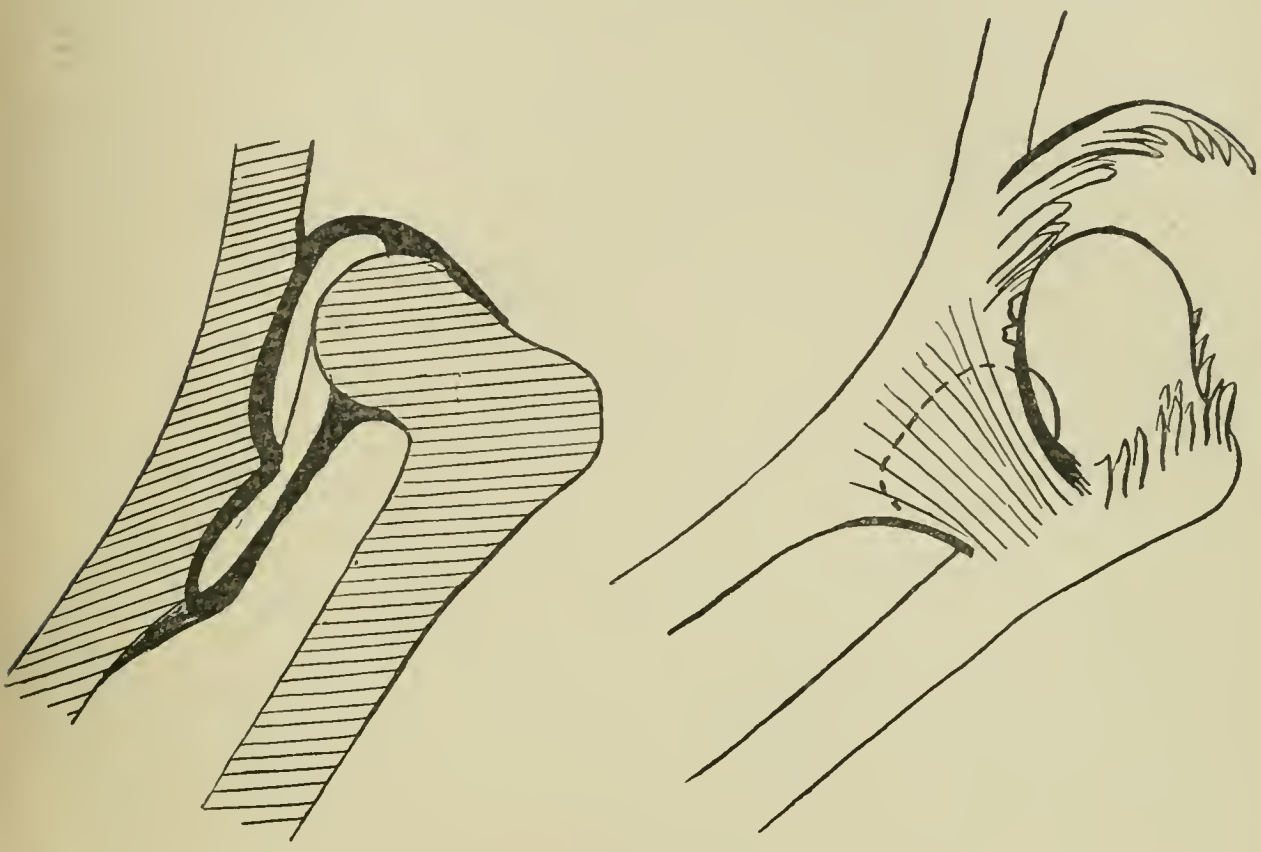


FIGURE 7.

Diagram illustrating difficulties in reduction of congenital dislocation of the hip. 1st. In the capsule covering the acetabulum. 2d. In the shortened capsule between the acetabular rim and the lesser trochanter.

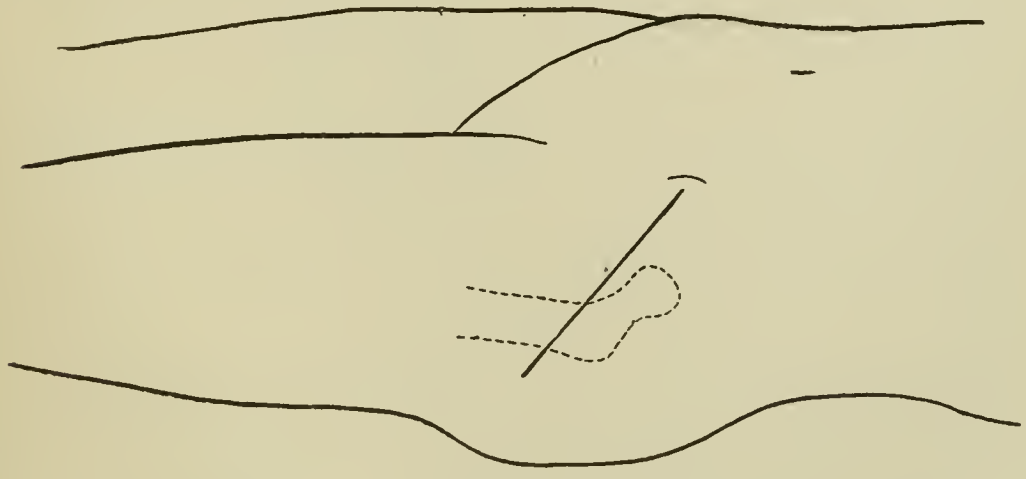


FIGURE 8.

Line of Incision for operative reduction.

the femur and should cross it slightly above the level of the trochanter minor. The tensor vaginæ femoris is retracted, and the fascia lata divided by a straight incision and, if necessary, by an additional cross incision. The gluteus is also retracted, and

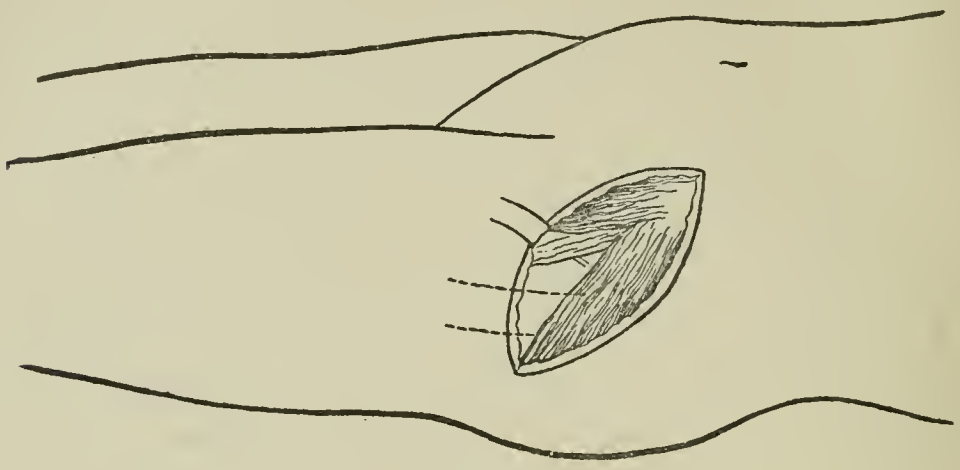


FIGURE 9.

Operative reduction—second step.

beneath the tensor muscle the rectus femoris will be found, with the reflected tendon passing outward to be inserted upon the ilium above the acetabulum. If the muscular tissues are well retracted the capsular ligament will be uncovered and can be split.

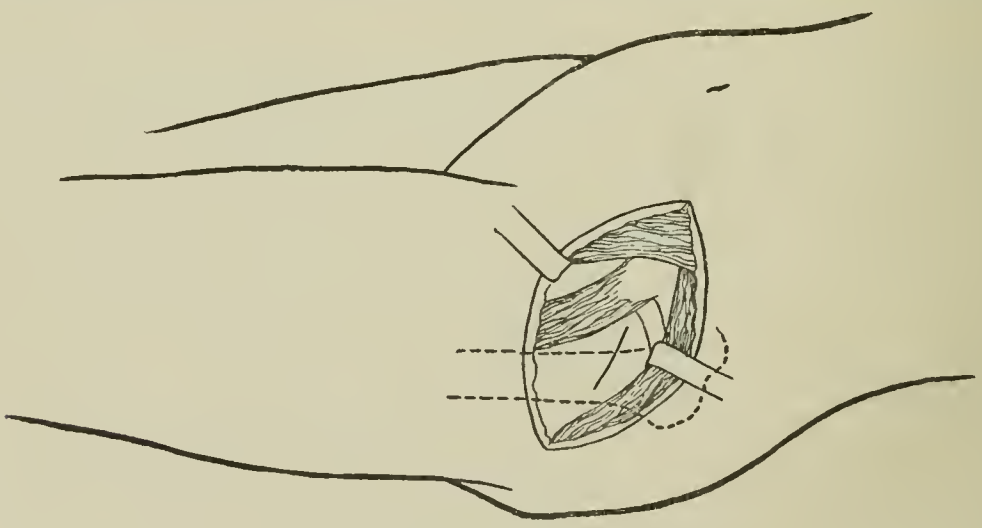


FIGURE 10.

Operative reduction—third step.

This should be done by an incision in the direction of the original skin incision and should be free enough to expose the whole head and neck as far as the trochanteric line. An assistant should flex the thigh to a right angle with the trunk, and the attachments of the

capsule to the neck and trochantic line, including the lesser trochanter, should be freed both on the anterior and posterior surface of the neck to such an extent that the surgeon can pass his forefinger completely around the neck. The head can then be thrown out and the ligamentum teres be divided, if present. The head of the femur can then be pulled aside and a clear view of the capsule covering the acetabulum, as well as the acetabulum, can be had. A curette can then be introduced to deepen the acetabulum, if necessary. It is important that the bony edge overhanging the

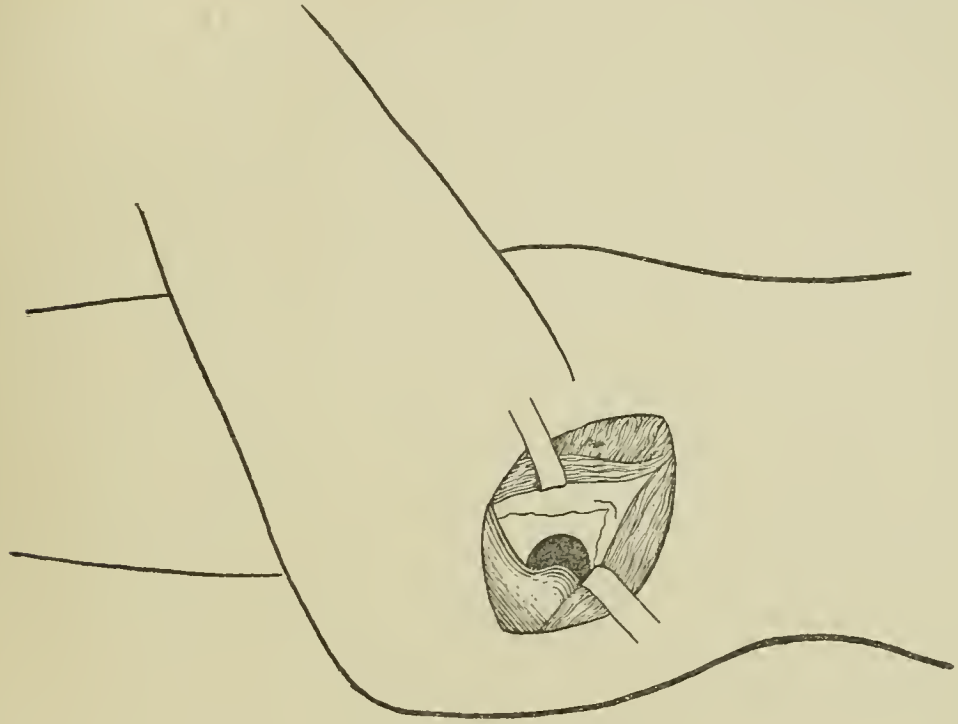


FIGURE 11.

Operative reduction—fourth step.

acetabulum should project sufficiently to furnish a firm socket after the head is reduced. It is sometimes difficult, if the tissues are imperfectly divided, to find the socket, for the reason that a portion of the capsule lies flat across the socket and is adherent to the edges, the surgeon feeling only the upper edge and a mass of connective tissue. This connective tissue must be divided in order to open the cavity. It is sometimes necessary, if the head of the femur is conical in shape, to remove a portion, but if the cartilage on the acetabulum is removed and the head of the femur freed from its cartilage, anchylosis is liable to result. It is particularly necessary that the capsule should not be folded, in attempted reduction, in such a way as to prevent the free entrance of the head into the

acetabulum, and it is especially important that the connection between the acetabulum and the femur at the trochanteric line and lesser trochanter should not be so firm as to prevent the reduction of the head into the socket. Where it is found that the head, when reduced into the socket, will not remain there if the leg is adducted or extended, some remaining fibres of the capsular attachments on the anterior surface passing from the ilium to the lesser trochanter and its adjacent parts, will be found to exist. After the acetabulum has been deepened sufficiently, the reduction of the dislocation should be performed.

Certain obstacles to reduction may be met, as follows: a thickened capsular fold above the neck of the acetabulum; narrowness of the constriction about the neck; undivided contraction of the capsule on the anterior and inner surface; contraction of the adductor muscles; a narrowness of the acetabulum. The manipulation necessary for the reduction differs from that usual in reduction of dislocation of the hip in that if the tissues are sufficiently stretched or divided, the head will be placed readily into the newly formed acetabulum. Where the head can be placed into the acetabulum with the leg somewhat abducted, the femur can be used as a lever to stretch such portions of the capsule as have been undivided by the knife. After the reduction the redundant capsule can be stitched with drainage, or packed, according to the judgment of the surgeon as to need of complete drainage. Drainage is of especial importance, as the cavity is a deep one and may be shut off in the process of repair by muscular contraction. Furthermore, in this region the danger of infection from urine, in some small children, is great. The limb should be flexed by means of a plaster of Paris spica reaching from the thorax down to the foot, holding the limb in a flexed and strongly abducted position, and a window cut through the bandage to the covered wound. The amount of abduction is dependent upon the amount of difficulty in retaining the head of the femur in the new acetabulum. The position of the limb can be gradually brought to normal by later application of plaster of Paris bandages.

ULTIMATE RESULTS.

Although the results of the earlier operations are not as favorable as those where added experience has taught the dangers and errors to be avoided, it is now thoroughly established that these cases can be cured by reposition through incision. This is not only

shown by the cases of Hoffa and Lorenz, but by the specimen from the patient operated upon by Delanglade. A child of three years with double congenital dislocation, six months after a successful operation upon one hip, died from measles before the second hip was operated upon. A complete cure was found to have been gained, the hip being placed in a well-formed socket. Hoffa reports 82 cases of reduction by incision, 30 of these being double, 52 single; 7 deaths, one during operation (chloroform?), one from intestinal catarrh, one from pneumonia, one from diphtheria, and the others from narcosis or shock. Of those who lived, there was a useful joint with from 1 to 3 cm. shortening in most cases, with good motion, though not full motion in all instances. There were 9 anchylosed cases, and 8 cases in which there was sepsis. Lorenz divides his cases into two series, the first, 12 cases in which there was suppuration and pus in 5; and a series of 100 later cases where there were excellent results with pus followed by anchylosis in only one instance. In 2 there was a slight fibrous adhesion. Delanglade reports 40 cases of reduction by incision, and 5 deaths from sepsis, with excellent results as far as could be determined in all, with the exception of two relapses. The mortality from sepsis would appear to be higher than thorough surgery would justify. It should be borne in mind that considerable difficulties are met in operating in this region, especially in children where the danger of soiling the dressings by urine is great. It is for this reason that Hoffa advises that the wound should never be sewn, but should be packed, and antiseptic rather than aseptic precautions be used. Where the wound was not sewn he had no trouble from sepsis. It is to be remembered that the wound is a deep one, and thorough drainage is not furnished by all incisions. It can, however, be expected that where drainage and antiseptic precautions are used, the danger from sepsis will disappear.

Schanz (Zeitschrift f. orthopadische Chirurgie, Bd. IV, Heft 2, p. 207) has collected 135 cases operated upon by twenty-one different operators.

Death occurred in seven cases; in four death followed from complication; in eight the result was unsatisfactory; in six the result was but partially satisfactory; in one hundred and nine the result was excellent.

Forcible Reposition.—The first case of an attempt at forcible reposition, under an anæsthetic, I have been able to find in congenital dislocation of the hip, is that performed by Dr. Post in 1884 and published in the report of the Boston City Hospital, where the

manipulations recommended by Bigelow for traumatic dislocation were done forcibly and the dislocation apparently reduced. (Report of the Boston City Hospital, 4th series.) A relapse, however, subsequently occurred. In 1888 the forcible reposition was recommended by Paci, and the method has been extensively discussed by continental surgeons. The method, however, lacked precision until Lorenz, whose experience in reduction by the aid of incision had given him a thorough knowledge of the pathology of the congenitally dislocated joint, suggested the so-called bloodless method. The method has now been employed by Lorenz, Hoffa, and others with permanent success, and with much less risk than that following reduction by incision. The operation has been proved successful in children younger than five, and in some cases in children as old as seven. The method recommended by Lorenz may be described as follows:

Before the operation, traction to stretch the muscles should be employed, combined with gradually increasing abduction. After a short time of this preliminary treatment, the patient should be anæsthetized and extreme force applied to the limb, with the thigh abducted. The child is placed upon its back and traction is exerted by means of a loop of yarn placed around the ankle and attached to a screw force fastened to the end of the table. Counter-traction is exerted by means of a long sheet of folded cloth placed beneath the perineum on the unaffected side. Force is slowly applied. The pelvis is tilted, and abduction is thus developed. This not only stretches the adductor muscles and the flexors, but also the hamstring and rectus femoris muscles, and the capsule which is firmly attached to the ilium, the shortened condition of which holds the femur in place. The ankle can be protected by sadlers' felt. If sufficient force is gradually applied, not only the capsular attachments stretch, but the head of the femur being pulled upon, the capsular neck is stretched. This can be still further enlarged if the stretched leg is forcibly moved from side to side in such a way that the head and neck may force their way through the acetabular pocket. After this procedure has been carried on for several minutes, accompanied by forcible manual stretching in the shape of massage of the adductor group, and aided possibly by a tenotomy of the adductors, forced circumduction of the thigh should be carried out. The different manœuvres for reduction of the hip should then be executed, flexion abduction and in and out rotation, varied in different cases, according to the obliquity or twist of the neck and the situation of the head. The exact manœuvre which

may be necessary can be determined if the hand of the operator is placed upon the head and its approach to the acetabulum determined. The reduction takes place with a noticeable jerk, as the head of the femur passes into the acetabulum, similar to what is seen in ordinary dislocation, but less marked. It will be frequently found that, after the reduction has taken place, dislocation will recur if the limb (previously strongly abducted and slightly flexed) is extended and adducted. This indicates that the anterior and inner attachments of the muscles and capsule are not sufficiently stretched, and would justify further attempts at stretching. As Lorenz has suggested, if the head is placed under the upper acetabular lip, the femur can be used as a lever to stretch the contracted tissues. After the reduction is thoroughly assured, the limb should be placed in a plaster of Paris spica, in a strongly flexed and abducted position, or, in other words, in such a position that the glutei muscles and the pelvi-trochanteric muscles can have a mechanical advantage over the flexor and adductor group. The amount of time the patient shall remain in this position will depend upon the amount of difficulty encountered in the reduction. Lorenz is undoubtedly correct, that if the patient is secured in such a way that flexion and adduction is not possible, the sooner locomotion is attempted, the better. In unilateral dislocation, the patient should be allowed to walk, fixed by a plaster spica, with the limb in an abducted position, within a few days, or as soon as the limb can be brought into such a position as to permit the patient to throw weight upon the limb. Where great resistance is encountered in the reduction, this may require a series of plaster bandages, some applied under an anæsthetic. After a while the fixed appliances may be removed, and a split spica can be employed, allowing massage of the muscles. If the unaffected limb is raised, the patient is obliged to walk with the affected limb abducted, which serves as a protection against recurrence. This also secures inward and upward pressure on the acetabulum. Treatment by manipulation and massage should be continued for several months, and the protective appliances gradually removed.

NOTE. I am greatly indebted to my colleague, Dr. Dane, for directions in regard to the method of bloodless reduction. He employed this method successfully in a case (a girl of seven, in my service) after having visited Prof. Hoffa and having witnessed several of his operations courteously shown him.

Minor modifications in the method may be found of use. As the important structure to offer resistance to complete reduction

is the anterior and inner portion of the capsule, or, in other words, that portion of the tissues which prevents forcible abduction, it is manifest that the direction in which the limb should be stretched is in the direction of abduction. If a child is placed upon its back on a frame, and by means of weight and pulley a slight traction is exerted with the legs abducted, it will be found that the amount of abduction can be gradually increased. A counter-pull can be made by means of cross straps pressing down upon the top of the trochanter, as is indicated in the accompanying illustration. (Fig. 12.) This can be done without causing the patient great discomfort, and a position of forced abduction, nearly at right angles with the trunk of the limb, can be gained in young children after a short time. Later, under an anæsthetic, a stretching appliance should be applied in such a manner as to stretch in an abducted position. A most efficient apparatus for this purpose is furnished by adding a windlass traction attachment to the well known Thomas knee-splint. At the upper end the attached ring presses upon the tuberosity of the ischium and the ramus of the pubes; at the lower portion a windlass with a long-handled crank is attached. This is connected with straps, fastened to adhesive plaster applied along and across the leg and thigh, and firmly bandaged to the limb. All desired power can be exerted, and the limb can be moved forcibly in the direction of abduction. The patient should be placed on the back, and the buttocks raised slightly by a pad. The traction appliance should be applied, and traction slowly used with the limb in as abducted a position as is possible. Under the traction, and with the help of the apparatus, abduction should be forcibly employed. This should be done until the axis of the limb is at a right, or even obtuse, angle with that of the trunk, in forcible abduction. After this, the limb should be stretched in the direction of hyper-extension under strong traction.

Greater precision is furnished by the mechanical arrangement for stretching here mentioned, but it is not always obtainable, and in its place manual force can be efficiently used in young children, or the hand, aided by a strap applied so as to pull the greater trochanter downward and inward, while the thigh is forcibly abducted. It should be remembered, however, that the manipulations needed in traumatic dislocation are not effective in congenital dislocation, the anatomical condition being different.

In reducing congenital dislocation, the limb should first be hyper-abducted, hyper-extended, as well as forcibly rotated, making room

Fig. 12.—Method of traction preliminary to operation in double congenital dislocation.

FIG. 12.

for the descent of a head by stretching the contracted capsule. If the stretching of the capsule can be thoroughly performed, a reduc-

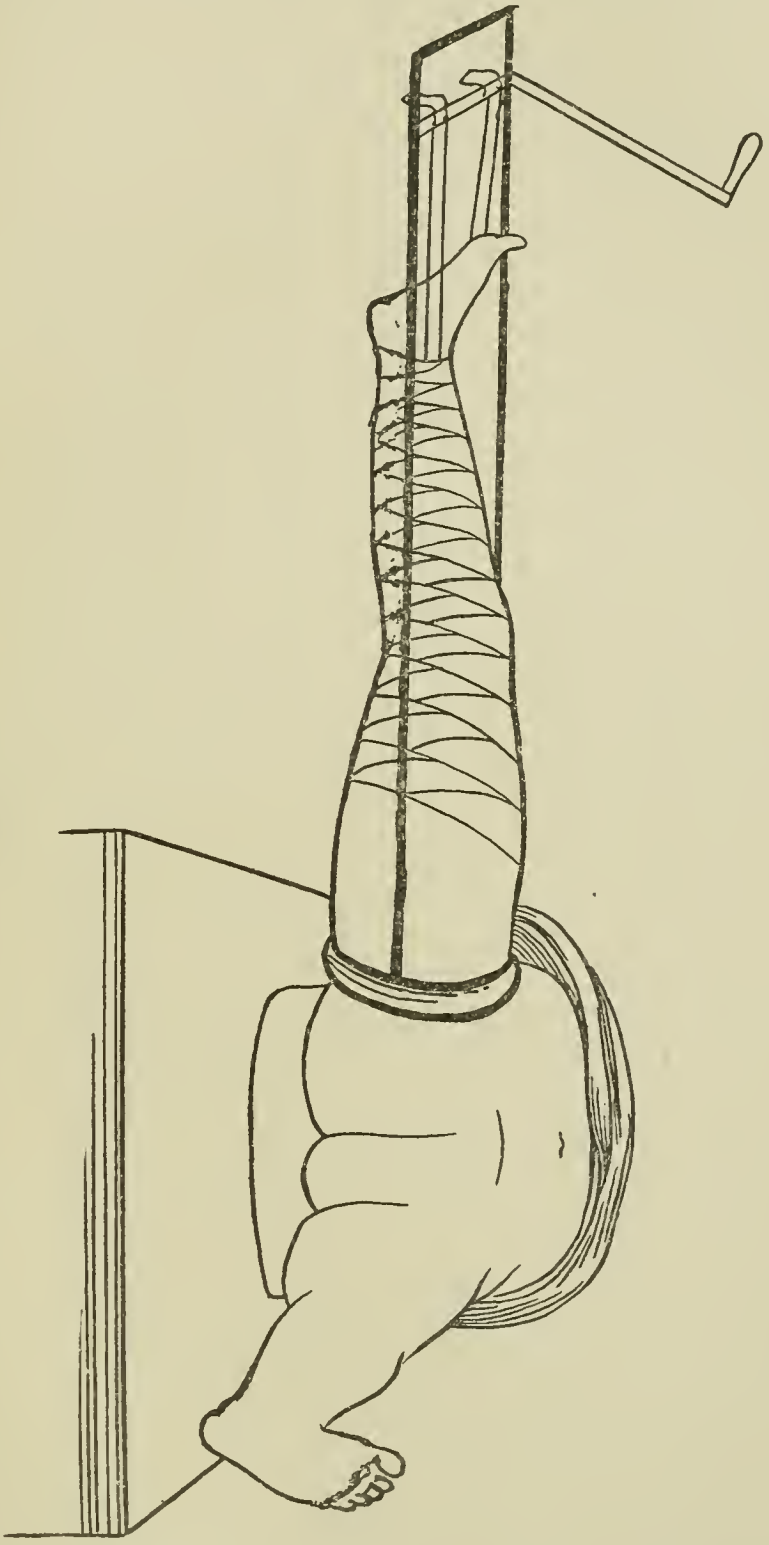


FIGURE 13.

Method of forcible stretching under anaesthesia with forcible abduction and forcible hyper-extension.

tion can be effected; if not, an incision is necessary. The procedure varies according to the amount of twist in the femur, as well as

according to other anatomical conditions, but it may be described as forced hyper-abduction, forced hyper-extension, forced circumduction followed by twisting the head into the acetabulum, the limb being somewhat flexed, abducted and rotated outward.

Neo Arthrosis Operation.—Where it is impossible to reduce the dislocation (and in the older cases the alteration in the capsule and the adhesions are so great that this is found practically out of the question) an operation has been proposed by Hoffa for the establishment of a new joint, based on the fact that in congenital dislocation there is no new formation of bone around the capsule, and that no true joint is established. Hoffa claims that it is impossible that the pressure of head should furnish sufficient irritation on the ileum for the establishment of a new and firm bony socket, as they are separated by an enormously thick capsule. He therefore recommends, in these cases, the opening of the capsule, and by means of the curette irritating the bone, after reducing the deformity as far as possible by means of traction, and using the contracted and shortened capsule in such a way as to prevent a free excursion of the bone upward when weight is thrown upon the limb. Although a few cases have been reported, the value of this method has not yet been thoroughly demonstrated. The unsuccessful cases of so-called Hoffa operation, where reduction after incision has not been effected, have been practically cases of neo arthrosis. It can be said that anything which will thicken and strengthen the capsule will be an advantage. It is also an advantage to change the dislocation from a posterior to an upward dislocation. The procedure for neo arthrosis must stand the test of time and further experience before adoption. It can, however, be hoped that, with the perfection of detail in surgical technique, older cases may be successfully operated upon than is at present true.

Excision of the head does not seem a proper procedure in congenital dislocation.

Generalizations as to the permanent value and limits of usefulness in operative reduction can perhaps not be made definitely before the next decade. It is certain, however, that in young subjects a reduction can be made, and although the immediate improvement in gait is not always at first as great as could be desired, the amount of improvement gained, as well as the certainty that a femur acting in its normal position will develop more normally than if dislocated, justifies the belief that the improvement in gait will be much greater in adult life than immediately after reduction. The

gait of middle-aged, or even adult, patients, operated upon when young, has yet to be determined, but it is probable that it will be normal. Reduction with incision is at present an operation to be performed, in all cases, between 7 and 15 years. The mortality and shock, as well as the relapses and stiffness observed in some cases, are largely due to imperfections in details, always incident to the introduction of a new method. They are, however, remediable, and will disappear as the operation is done more rapidly and antiseptic details are more thoroughly carried out. Excellence in the result will depend upon the amount of deformity remaining in the neck of the femur. This in younger cases will be less than in older, but even in older cases a subsequently osteotomy of the neck of the femur, such as is used in coxavara, may be expected to give an increased improvement in gait.

Mechanical Treatment.—It would seem as if the gradual reduction of a congenital dislocation of the hip into a loosely-formed socket should be an easy one. Experience, however, belies such an opinion. One difficulty, apart from overcoming the muscular contraction, lies in the fact that a traction force which is exerted without an anæsthetic, without sufficiently stretching the capsular attachments to the ileum, pulls the head past the opening into the acetabular pocket, and leaves an interposing thick capsular covering, which prevents the entrance of the head into the socket. It has been supposed that manipulation would force the head of the femur into the forming of a new acetabulum, but that opinion is based upon a false supposition of the pathological conditions. It is irrational to suppose that the head of the femur would force its way through a structure almost as firm as the tendo-Achillis. There may be instances where the capsular neck is wide, and the head would easily drop into the proper position, but clinical experience does not support such a belief. Positive and enduring success under mechanical treatment has yet to be demonstrated by clinical evidence.

But even if it is doubtful if any case has been completely reduced under gradual stretching, it is possible in the future that this may be done by means of a traction force in the position of forced abduction, which will thoroughly stretch the flexor and adductor muscles and the capsule, and later twisting the head through a widened capsular neck into the acetabulum. Any weakening of the joint could be overcome in time under graded and protected use of the limb. An attempt of the sort would only be justifiable in very young chil-

dren, but at present no surgeon would be warranted in attempting it for a period longer than a few weeks.

Palliative Measures.—As palliative measures are recommended in the shape of traction appliances and corsets, where for any reason operative treatment is impossible and improvement all that can be aimed at, the question of the most rational means of improvement is a proper one, with the value of which a surgeon should be familiar. It is clear that any method which will shorten the lengthened capsule and lengthen the shortened muscles will be of advantage, but It is clear that any method which will shorten the lengthened capamount of benefit which can be expected is not great, but in the cases who have worn apparatus of this sort noticeable improvement in gait can be observed.

To express it figuratively, the body of a carriage slung on the truck would hang higher, if the straps which sustain the weight were shortened. A Thomas knee-splint furnished with traction meets the indications of a downward pull, and its use in young children will be found to lengthen the limb and interfere with the child's freedom in play and locomotion but slightly; lengthening of the limb can be obtained and maintained, and it is probable that in time the soft tissues will be altered. Corsets improve the patient's carriage and check the tendency to lordosis while they are worn; if accompanied by proper gymnastic exercises, it cannot be thought that they interfere materially with the muscular development, provided massage is employed. A simple form of corset to be applied can be made as follows: A cast is taken of the patient's trunk and hip under moderate extension. This can be taken in the recumbent or in the suspended position. The corset should be made from this cast, passing well down upon the hips. The corset can be made of cloth, leather or stiffened paper, or a combination of these. The leather or cloth should be re-enforced by steels. The object of such a corset is to exert a forward pressure on the back between the shoulders and on the lower portion of the sacrum, and a backward pressure over abdomen. Such a corset can be made to furnish a downward pressure upon the trochanter. This can be aided by the use of perineal straps.

My personal experience in the treatment of congenital dislocation of the hip can be divided into three classes:

Class 1. The mechanical treatment. 8 cases. In one the treatment was continued thoroughly according to the Guerin and Buckminster Brown method, with three years of recumbent

Fig. 14.—Child 4 years old, showing profile of the back after operative reposition (anterior incision) in single congenital dislocation of the hip.

FIG. 14.

Fig. 15.—Child 7 years old, after forcible reposition in single congenital dislocation of hip, showing absence of lordosis.

FIG. 15.

traction, followed by a corset and apparatus. In none of these cases can the results be considered as satisfactory, and the treatment may be regarded as palliative. Several of the cases have been watched for eight years; and in one, the gait after treatment by massage and gymnastics is excellent, though considerable lordosis remains. One case, a girl of 16, had undergone thorough treatment when a young child by recumbent traction and manipulation for several years with a supposed cure; a relapse after puberty had taken place at the time the patient presented herself to me.

Class 2. Operations by the Hoffa method, with the Langenbeck incision. 6 cases, 2 being double. Recovery from the operation in 4. The ultimate results in these cases, however, were not satisfactory. One died five weeks after the operation, during an epidemic of naso-pharyngeal diphtheria, suppuration occurring in the wound before death. Death in another case followed in six weeks after recovery from the operation, with the wound healed, from scarlet fever; and in a third case, a month after the wound healed, from an unknown cause, with dysenteric symptoms. In the 3 remaining cases, one being double, but little improvement followed in gait (although complete recovery from the operation took place), and the head was in all probability not thoroughly reduced into the acetabulum, as it was not firmly fixed and some lordosis remained.

Class 3. 5 later cases. Operation performed by a Lorenz anterior incision. The head was reduced in 4 of these, one being at present under observation; in the fifth case, a girl of 15, the head was not reduced, suppuration followed, the girl recovered with a useful, but not improved, limb.

Class 4. Reduction by forcible manipulation. 4 cases. 2 cases in which 12 years ago an imperfect attempt at forcible reduction by the Post method was made unsuccessfully; 2 later cases, one double, treated successfully. In one, of the age of seven, single dislocation, the reduction was performed by Dr. Dane employing the Lorenz method. In the second, a child of 3 with double dislocation, reduction was effected by means of forcible splint traction.

Class 5. 3 adults (single dislocation) treated for attacks of severe muscular pain. Treatment by means of rest, local application of heat, massage, electricity, and the temporary use of crutches. The patients recovered from the attacks after a period of discomfort varying from 2 weeks to 6 months.

CONCLUSIONS.

Congenital dislocation of the hip is a dislocation of the head of the femur upwards, occurring in uterine life.

A shallow triangular acetabulum results.

A diminution of the angle between the neck and shaft takes place and a twist of the neck.

The capsule is altered by being stretched, thickened, first dilated in its upper portion, stretched across the acetabulum in the lower portion, and constricted at the rim of the acetabulum.

The most important obstacle to reduction lies in the attachment of the capsule, displaced and thickened, to the ileum above and around the front of the acetabulum and to the anterior surface of the femur, especially to the lesser trochanter.

The shortened pelvi femoral muscles also offer a resistance to reduction, and with the contracted capsule will prevent reduction or cause relapse.

Obstacles to the reduction of deformity also lie in the shape of the head and in the shallowness of the acetabulum.

Traction in a straight direction cannot effect a cure.

Traction in strong abduction, with downward pressure upon the head, may bring about reduction.

In children over two and under five—in some instances between five and seven— under an anæsthetic, forcible reduction can be successfully used. This can only be accomplished if the head of the femur is forced into and through the capsular neck, dilating it, and into the acetabulum, and only after the capsular attachments adducting and flexing the limb are thoroughly stretched.

Successful reduction is always accompanied by an audible movement of the head of the femur into the capsule, and bandages and fixation apparatus are to be used to prevent relapse, until the contracted tissues are sufficiently long and the pelvic trochanter muscles have regained their power to a sufficient extent that a recurrence of the dislocation is impossible.

In cases older than seven and under fifteen, and in some cases between five and seven, an open incision is necessary for reduction of the dislocation.

The line of incision following the outer edge of the tensor vaginæ femoris is the preferable incision.

Inability to reduce the head is due to capsular attachments from the acetabulum and ilium to the femur, which have not yet been divided or stretched.

In old adolescents, or adults, where extensive alteration in the bone takes place, operative reduction has not been successful.

The use of corsets and traction splints may improve attitude, but cannot cure.

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Paper in DISCUSSION,

BY DR. VIRGIL P. GIBNEY, of New York.

From a careful study of the methods employed during the past decade for correcting this deformity, I am convinced that a perfect method has not as yet been devised.

In my own opinions I have followed Hoffa and Lorenz in their bloody reduction, and while I am able to report a certain amount of improvement in a good number, I am sure that none have been cured—employing this much abused term in the sense of perfect restoration of function and free from any shortening. To be a little more explicit, I am not familiar with any result that has left the patient free from a limp and with a hip that is equal to a normal hip.

In some instances the improvement in gait has been so marked that we are led to believe this lameness will decrease in time so that the disability will be practically insignificant. Yet in these cases that time has not yet arrived.

In a certain proportion of the cases operated upon I am sure the deformity and the shortening and the lameness have been increased.

The more recent operations have been preceded by a few weeks of traction in bed, thus rendering unnecessary the extensive cutting of tissues about the hip and making the reposition of the head much easier. I have been disappointed, however, in the results obtained, and am unwilling to give these as final results; for the reason that in the earlier cases, instances have occurred in which the disability has seemed to recur two or three years after a fair result was thought to have been obtained.

Two or three of my operations have been followed by an arthritis which closely resembles the arthritis met with in suppurative tuberculous ostitis of the hip.

The general surgeon has not been convinced that either Hoffa's or Lorenz' operation is to be commended. He is willing to mildly approve in certain young subjects, yet it is safe to say that he is not at all enthusiastic.

One cannot claim that the subject has not been sufficiently discussed and the operations adequately elucidated, both in this country and on the Continent, for the report is current that German surgical societies have passed resolutions prohibiting papers and discussions on congenital dislocation of the hip for the next two years.

Having thus expressed myself as not at all satisfied with the open method treatment, I feel that much may be said in favor of the more recent treatment advocated by Prof. Lorenz, which differs in some respects from that advocated by Paci.

The theory that the head of the bone crowded into the rudimentary acetabulum will, if this crowding can be continued in the right direction, make a cavity sufficiently deep to be serviceable, is certainly worthy of credence, but as yet actual facts are not forthcoming.

The absence of a cutting appeals to the lay-minded, and I am positive that many cases will be subjected to this procedure.

It may not be amiss, in this discussion, to call attention to the facility with which children of congenital dislocation of the hip get about. Where both hips are displaced the gait is comparatively easy. It is waddling, it is true, but then a great many children learn to walk with this peculiar gait very much lessened, so to speak. They obtain certain control of the muscles which make a firm bearing, against which the head of the bone is brought in walking. In all my experience, extending now over 25 years, and with an opportunity of seeing half a dozen of these cases every year during this period, I am convinced that very few suffer any after the effects of the displacement.

I recall one case in a lady about 35 years of age, who had grown stout, and whose hip then began to give her some pain and discomfort. An abdominal belt, so constructed as to distribute the force of the head of the bone throughout the gluteal region, with some little counter irritation, gave relief and she was able to dispense with the support later and had no recurrence of the pains. In one-sided dislocation, of course, the gait is very awkward and the limp is always present. If we can devise an operation that will do away with this limp or reduce it to a minimum, then I feel that a certain risk may be taken and I so advise my patients, but until we can arrive at an operation or mode of reduction that will do away with this limp and enable us to assure the patients that a relapse will not occur later in life, until we can do this, I say, I feel that the cutting operations, known as the open or bloody method, should be abandoned. I see no objection to resorting to the last operation advised by Lorenz, and I shall certainly make efforts in this direction.

Paper by Dr. Harry M. Sherman, San Francisco, Cal.

It will, perhaps, be best to preface what I wish to say by a brief description of the operation for reposition as I saw Lorenz do it. My recollection of it differs a little from Dr. Bradford's description, and this is probably due to later changes on the part of Lorenz. The child was always fastened to the table by a folded sheet between the thighs, the ends passing up to the head of the table and being made fast there. This gave efficient counter-traction. There was put around the ankle a loop of a thick yarn strand, for the direct traction. The first step of the operation proper was the subcutaneous section of the adductor tendons. The incision which gave access to the acetabulum was made along the anterior border of the tensor vaginæ femoris muscle, between that and the rectus. After the incision had been carried down through the fascia lata, the field of the operation was beyond where one could see, but it was evident that the incision was carried down through the capsule by the scalpel. The capsule was then very freely incised by a larger, blunt-pointed, long-handled tenotome, so that the head could be easily drawn down from its false position on the dorsum. Then the acetabulum was located and, by means of a gouge, guided by the finger in the wound, its cavity was deepened and enlarged, so that it would receive and retain the femoral head. By traction and manipulation the head was put in the acetabulum, a small gauze drain arranged, and a skin suture made.

Now comes the part that, to me, seems most important. Lorenz put the case up in a plaster of Paris spica, with the leg extended and very much abducted. This held the head more firmly in the acetabulum than could any other position, because in all these cases it is possible to reproduce the dislocation by simply adducting the leg and moving it a little. He kept the patient in the spica for six weeks, taking off portions of it at times, until by the end of six weeks it was all off and the child was allowed to get up and walk.

It has been a puzzle to many of us to locate the acetabulum, the attempts to do so by landmarks from the outside having often failed. I think it can always be easily found if this plan be followed. It is known that the capsule is never perforated by the femoral head, nor is it separated from its attachments to the rim of the acetabulum. The finger then, passed into the incision

in the capsule to the head, can be made to traverse the capsule downward and forward directly into the shallow acetabulum. With this finger as a guide, the capsule may be further slit so that the gouges may have easy access.

After the splints have been taken off my own cases I have always found easy motion in the joint, though in a limited range; but later the range of motion is lessened and a certain postural deformity develops, the limb passing over into the position of flexion and adduction. Lorenz combats this tendency by beginning at once systematic treatment by massage and passive and active motion, so that the maximum of motion is gotten in the minimum of time. The consideration of the conditions in the joint and this resulting deformity has led me to believe that it can be aptly compared to the joint conditions and the deformity of a healed case of hip joint disease. Certainly there are definite points of similarity between the two. In hip joint disease we have the femoral neck and head depressed and shortened by the pathologic destruction and absorption; in congenital dislocation the neck is twisted forward and downward, and the head is often small and misshapen; so that in each case there is shortening and deformity. In hip joint disease there is frequently an acetabulum enlarged, by pathologic absorption also, in its upper portion; in congenital dislocation the acetabulum, in the process of enlargement by gouging, may be made to occupy too high a place on the ilium. In healed hip joint cases there is always a certain amount of cicatricial tissue in the capsule, and the same condition exists in the dislocation cases that have been submitted to operation. In hip joint disease, again, the muscles may have been affected to the point of the abductors having been destroyed by abscess sinuses; in congenital dislocation the abductors are weak, because of the pressure of the dislocated femoral head among them, and also because, until the head of the bone has been put into the acetabulum, they have had no leverage to work on, and have consequently been practically functionless. Meanwhile, however, the adductors have been, in both instances, functionating, for they are always adductors, no matter what the position of the limb, or the location of the head of the bone. So these two originally dissimilar conditions may resemble each other in the deformities of their final stages, because of similar mechanical and vital conditions.

In my own cases I have not had practiced the massage, and in one case I saw the deformity of rigid flexion and adduction develop,

and then,—as I thought, in response to use and the gradual increase of strength of the abductors—the position of the limb improved, the adduction and flexion lessening; so that it is possible that even without those six months of tiresome treatment we may be able to get satisfactory results.

As to what is to be the ultimate result of the procedure, we must wait some years to find out. I am satisfied with the results of the first six months after treatment. These results are more striking if they can be seen in a case of bilateral dislocation, where one side only has been subjected to operation. The stability and poise of the trunk, when the patients step on the operated-on leg, is in marked contrast to the swaying and weak step of the still dislocated side. I do not know of any mutilation in the operation which might interfere with subsequent development, and I believe that we are justified in assuming that, if the early results are as good as those I have seen, the later ones should be equally so. A great deal will depend on the technical skill of the operator, for it is one of the operations the frequent repetition of which is necessary to insure precision and rapidity of manipulation and the avoidance of sepsis. The occurrence of the latter is most deplorable, for these cases are exceeding unhappy ones to have suppurate, as the chance of satisfactory joint motion is jeopardized.

I do not know what to say about the bloodless operation. I never saw it done, but I saw a case of bilateral dislocation in which Lorenz had done it and he had had it up in apparatus, with the legs abducted to a right angle with the trunk. He could, at the time I saw the case, pull them carefully down to the proper position without re-dislocation. Another case of his had had a one-sided dislocation, the bloodless method had been practiced and the child was running about with a tall shoe on the sound side, so that by the tilt of the pelvis the leg that had been dislocated would be kept at its work in a slightly abducted position. In examining this case, I doubted if the head was in the acetabulum. I was sure I felt it just below the anterior superior spinous process, and that the dislocation had been changed from a posterior to an anterior one. I know now what a very shallow thing the acetabulum is, and that the femoral head can be easily felt, even though it is in the socket, and it may be that in Lorenz's case I was mistaken in thinking it an anterior misplacement. Even if it was a translation of a posterior into an anterior dislocation, the case had been much improved by the procedure.

I saw but a little while ago a woman who had a bilateral case, posterior position of the heads. She was married, had borne children and was getting stout, and walking was becoming progressively more difficult. The increasing helplessness that was being imposed upon a perfectly healthy woman by this deformity was an object lesson to me, and impressed on me the necessity of devising means for the relief of the disability. I feel confident that we are on the right road to the accomplishment of that, and that with some more experience we shall be able to replace in the acetabulum, either by manipulation, or by cutting operation, the heads of all misplaced femora.

ACUTE GENERAL PERITONITIS.

CLASSIFICATION.

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An intelligent and systematic discussion of acute peritonitis must be necessarily based on a rational classification. A great deal that has been said and written on this subject from the distant past until the present time is worthless from a scientific as well as a practical standpoint, owing to a lack of a proper classification. The ordinary terms used to designate the different forms of peritonitis are differently interpreted and applied by pathologists and clinicians. Acute inflammation of the peritoneum is produced by so many different causes and assumes such varied clinical aspects that renders it extremely difficult to formulate a satisfactory classification. A discussion of the etiology, differential diagnosis, prognosis and treatment of acute peritonitis, except upon the basis of a clear and comprehensive classification, is fruitless, misleading and usually results in the deduction of erroneous and often dangerous conclusions. The classification should include the anatomy, pathology and etiology of the disease, to be of value in rendering a correct diagnosis, and in enabling the physician and surgeon to advise and apply effective therapeutic measures.

I. ANATOMICAL CLASSIFICATION.

An accurate anatomical diagnosis is necessary for the purpose of locating the inflammatory process correctly, or to trace the connection between it and the organ primarily the seat of infection. During the beginning of the attack, and in cases of localized peritonitis, the inflammation can usually be located without much difficulty, while the reverse is often the case after the disease has become diffuse. The inflammation may commence and spread from either surface of the serous membrane, visceral and parietal.

a. Ecto-peritonitis. An inflammation of the attached side of the peritoneum is called ecto-peritonitis. As compared with inflammation of the serous surface, this inflammation of the subendothelial vascular connective tissue is characterized clinically and

pathologically by intrinsic tendencies to limitation of the inflammatory process. The mechanical and anatomical conditions for diffusion of the infection are less favorable than when the free surface of the membrane is affected. Ecto-peritonitis, however, in certain localities may become quite diffuse when the cavum Retzii (Wm. Gruber) or the retro-peritoneal space on either side of the spinal column is the seat of a suppurative inflammation. In the latter locality a paranephric or spondylitic abscess is often the cause of an extended ecto-peritonitis, the extent of the disease corresponding with the size of the subperitoneal abscess. In infected wounds of any part of the abdominal wall in which the peritoneum is exposed but not perforated, the primary ecto-peritonitis is occasionally followed by the extension of the infection to the serous surface through the lymphatics, or the direct extension of the infective process through the tissues until it reaches the endothelial lining. Peritonitis of a visceral origin is always preceded by ecto-peritonitis, whether the infection reaches the peritoneal cavity through a perforation or by progressive extension of the infection from the primary focus through the tissues until it reaches the free peritoneal surface.

b. Endo-peritonitis. What is usually spoken of and described as peritonitis is an inflammation of the serous surface of the peritoneum which, anatomically speaking, is an endo-peritonitis. Endo-peritonitis not infrequently leads to ecto-peritonitis and the formation of subserous abscesses. In inflammation of the serous coat of the intestines the peritoneum is always loosened and frequently extensively detached by the secondary ecto-peritonitis.

c. Parietal Peritonitis. Inflammation of the serous lining of the peritoneal cavity is called parietal peritonitis. It may occur as a primary affection in penetrating wounds of the abdomen, but more frequently it is met with as a secondary disease, in consequence of the extension of an infection from one of the abdominal or pelvic viscera, or perforation into the peritoneal cavity of a visceral ulcer or a subserous or visceral abscess. Visceral peritonitis is always associated with parietal peritonitis, and parietal peritonitis is only absent in visceral peritonitis when the inflammation remains limited and the parietal peritoneum is protected against infection by plastic exudations. In the female parietal peritonitis of the pelvic floor usually follows in the course of an extension of an infective process from the internal genital organs through the lymphatics, rupture of a visceral or connective tissue abscess into the peritoneal cavity, or leakage of septic material from the Fallopian tubes.

d. Visceral Peritonitis. Inflammation of the peritoneal investment of any of the abdominal or pelvic organs is known as visceral peritonitis. The inflammatory process is seldom limited to a single organ, as during the course of the disease adjacent organs or the parietal peritoneum will surely become involved. In diffuse peritonitis the whole peritoneal sac and the serous covering of all of the abdominal organs are affected. The nomenclature of visceral peritonitis is a lengthy one, as it includes all of the abdominal and pelvic organs from which, when the seat of a suppurative inflammation, may become the primary starting-point of an attack of localized or diffuse peritonitis. The mesentery and omentum are modified anatomical forms of the peritoneum, and when the seat of inflammation we speak of mesenteritis and epiploitis. Peritonitis involving the serous covering of any abdominal organ and arising in consequence of an inflammation of the organ which it invests, is designated by the prefix *peri*, and the noun used to indicate the organ primarily affected in a state of inflammation, which has given rise to the following terms: peri-gastritis, peri-enteritis, peri-typhlitis, peri-appendicitis, peri-colitis, peri-hepatitis, peri-splenitis, peri-cystitis, peri-salpingitis, and peri-oöphoritis.

e. Pelvic Peritonitis. Inflammation limited to the peritoneal lining of the pelvis and its contents is known clinically and anatomically as pelvic peritonitis. It is an affection almost entirely limited to the female sex, and in the majority of cases is caused by extension of gonorrhœal infection from the Fallopian tubes, or a mild form of pyogenic infection from the uterus, its adnexa, or connective tissue of the parametrium.

f. Diaphragmatic Peritonitis. Inflammation of the under surface of the diaphragm is described as diaphragmatic peritonitis, and when it assumes a suppurative type and remains limited leads to the formation of a subdiaphragmatic abscess. This acute localized form of peritonitis is usually secondary to suppurative affections of the liver and gall bladder and perforating ulcers of the stomach and duodenum.

2. ETIOLOGICAL CLASSIFICATION.

The classification of peritonitis upon an etiological basis is of the greatest importance and practical value. The nature of the exciting cause frequently determines the anatomical and pathological varieties. It likewise has a strong bearing upon the prognosis and often furnishes positive indications as to the methods of treatment

that should be adopted. Peritonitis, like every other inflammatory infection, is always the result of infection with pathogenic microbes, usually of the pyogenic variety. The etiology must consider the different avenues through which the microbes find their way into the peritoneal cavity.

a. Traumatic Peritonitis. Primary peritonitis has usually a traumatic origin, that is, the injury establishes between the peritoneal cavity and the surface of the body or some of the hollow abdominal or pelvic organs a communication, through which pyogenic bacteria enter in sufficient quantity and adequate virulence to cause an acute inflammation. Traumatic peritonitis is most frequently caused by penetrating wounds of the abdominal wall, the uterus and lower portion of the œsophagus. In some cases, penetrating wounds of the chest extend into the abdominal cavity through the diaphragm. Contusions and lacerations of the abdominal organs often cause peritonitis by extravasation of the secretions or excretions of the injured organ. Not infrequently the injury is followed by a circumscribed suppurative inflammation in the injured organ, which later is followed by diffuse peritonitis from perforation of an abscess, or the injured wall of any part of the gastro-intestinal canal, in which case the peritonitis follows as a secondary affection.

b. Idiopathic Peritonitis. The occurrence of peritonitis without an antecedent injury or suppurative lesion is doubted by many. It is an exceedingly rare affection, since pathologists and surgeons have brought, by their investigations and observations, the peritoneal inflammation, with few exceptions, in connection with a neighboring or distant primary suppurative lesion. It is certainly much more rare than primary inflammation of the pleura and pericardium. It is too early to deny *in toto* the existence of so-called idiopathic peritonitis, but future bacteriological examinations of the inflammatory product will, no doubt, reveal a microbic cause in all such cases. Leyden found, in a case of primary peritonitis in the inflammatory exudate, diplo- and strepto-cocci. As an isolated affection, peritonitis is found most frequently in females during or soon after menstruation. It is probable that the pyogenic bacteria multiply in the blood which accumulates in the uterus and reach the peritoneal cavity through the Fallopian tubes. It is said to have occurred in consequence of exposure to cold, and is then known as rheumatic peritonitis. Occasionally it has been observed as one of the remote manifestations of Bright's disease, pyæmia and the acute eruptive fevers.

c. Perforative Peritonitis. Perforation of an ulcer of any part of the gastro-intestinal canal, or of an abscess of any of the abdominal or pelvic organs, or of the abdominal wall into the peritoneal cavity, is by far the most frequent cause of acute peritonitis. Two important and frequent causes are appendicitis and suppurative salpingitis. If localized inflammation develops over the ulcer or abscess before perforation takes place, the general peritoneal cavity is often protected by firm adhesions before the accident occurs, and the peritonitis remains circumscribed. If, however, the contents of the gastro-intestinal canal or the abscess cavity reach the free peritoneal cavity, a diffuse septic peritonitis sets in, which usually destroys life within from twelve to seventy-two hours unless prompt surgical treatment is resorted to. Experimental research, as well as clinical observations, have demonstrated that the intestinal wall, when paretic or gangrenous, becomes permeable to the microbes contained in the intestinal canal. In many cases of intestinal obstruction, acute and chronic, death results from septic peritonitis after the intestine has become paretic or gangrenous.

d. Metastatic Peritonitis. This form of peritonitis occurs, like other metastatic affections, in connection with a suppurative or infectious process disconnected from the peritoneum. It is more rare than metastatic pleuritis, and is seldom seen except as a pyæmic lesion. In very rare cases it develops in the course of many of the acute infectious diseases, as scarlatina, smallpox, erysipelas, rubeola, and even varicella. It also occurs frequently in the course of septicæmia and pyæmia. Andral and Desplatz have seen it occur during attacks of acute articular rheumatism. It has also been observed in scorbutic subjects and patients suffering from valvular disease of the heart.

e. Puerperal Peritonitis. Peritonitis occurring in connection with septic diseases of the puerperal uterus has for a long time been known as puerperal peritonitis. The infection may extend from the endometrium through the Fallopian tubes, or it may follow the lymph channels or the thrombosed infected uterine veins. Infection through the lymphatics usually results in rapidly fatal, diffuse, septic peritonitis, while in thrombo-phlebitis there is a greater tendency to localization, unless the thrombi disintegrate and cause embolism and pyæmia.

f. Peritonitis Infantum. Peritonitis attacks most frequently children, young adults and women during the child-bearing period of life, but no age is exempt.

g. Fœtal and Intrauterine Peritonitis. If the disease attacks, as it occasionally does, the fœtus in utero, it often results in death before, or soon after, the birth of the child, most frequently death ensues during the seventh to the ninth month of gestation. Prenatal peritonitis is frequently associated with syphilis. In most cases the disease is only detected at the post-mortem; in others death, if the child is born alive, is preceded by meteorism, icterus, and œdema of the legs.

h. Peritonitis Neonatorum. Infection takes place during the first few weeks after birth through the imperfectly healed ulcerating umbilicus. It has been met with most frequently in children whose mothers were afflicted with puerperal fever. Besides peritonitis, symptoms of pyæmia appear.

3. PATHOLOGICAL CLASSIFICATION.

The pathological conditions which characterize the different varieties of peritonitis must necessarily be considered in classifying this disease. The pathological classification is based almost entirely upon the gross and microscopical appearances of the inflammatory exudation and transudation.

a. Diffuse Septic Peritonitis. Every acute peritonitis is septic, in so far that phlogistic substances reach the general circulation from the inflammatory lesion, and in that frequently the inflammation terminates in suppuration, but the term septic peritonitis should be limited to those cases of acute septic peritonitis in which, as a rule, death occurs in a few days and before any gross pathological conditions have had time to form. It is a disease that is almost uniformly fatal, with or without operative treatment, the patients dying from the effects of progressive sepsis. The claim of operators, to have cured such cases by laparotomy, must be accepted with a good deal of allowance. The microbes which produce this form of peritonitis are those which follow the lymph spaces and are rapidly diffused, not only over the entire peritoneal surface, parietal and visceral, but also through the subserous lymphatic channels. The disease is observed most frequently after perforation into the free peritoneal cavity of an abscess containing septic pus, rupture, or perforation of any of the abdominal or pelvic viscera containing septic material, gunshot or stab wounds of the abdomen with visceral injury of the gastro-intestinal canal, and occasionally as the result of infection during a laparotomy. The gravest form of puerperal fever is a diffuse septic peritonitis.

The subjects of this variety of peritonitis die so soon after the beginning of the disease, that at the post-mortem, or if the abdomen is opened during life, at the operation, no gross tissue changes are discovered. Besides a slightly increased vascularity, nothing is found to indicate the existence of peritonitis. The septic material, formed in large quantities and of great virulence, is rapidly absorbed by the stomata of the under surface of the diaphragm discovered and described by von Recklinghausen.

b. Putrid Peritonitis. The inflammatory product in this form of peritonitis is a scanty brown, or reddish brown, fluid. It occurs most frequently in connection with grave forms of puerperal metritis. It is usually associated with more or less gangrene or ulceration of the organ, or parts primarily affected, as uterus, intestine, or abdominal wall. Gasogenic putrefactive bacilli are frequently found in the inflammatory product.

c. Hemorrhagic Peritonitis. The ascites, which so frequently develops in consequence of malignant or tubercular disease of the peritoneum, is composed of serum frequently stained with blood, but in acute peritonitis the transudate is occasionally hemorrhagic by the tearing of vascular adhesions, and rhexis is also observed in persons suffering from peritonitis that are greatly debilitated, scorbutic or intemperate, and occasionally when peritonitis occurs in patients suffering from typhoid fever. It is met with most frequently in the pelvis upon the posterior surface of the uterus and vagina, and in men behind the bladder. The inflammatory product appears in the form of brown patches, which are composed of delicate and very vascular villi. These villi, from their unfavorable location, are subjected to frequent mechanical disturbances, and when injured bleed, giving rise to the so-called retrouterine or retrovesical hæmatocele.

d. Suppurative Peritonitis. Suppurative peritonitis, that is, an inflammation of the peritoneum which results in the formation of pus, is always more or less circumscribed. This form of peritonitis is the most frequent, and is generally associated with more or less fibrinoplastic exudation. The pus is either serous, sero-purulent, or may reach the consistence of cream, when it is usually of a yellow color. The accumulation of pus may be so large that upon opening the abdominal cavity it may appear as though the entire peritoneal cavity and all of the organs contained within were implicated, but a careful examination will almost always reveal the fact that a large part of the peritoneal cavity and many of the organs were shut out from the inflammatory process by plastic adhesions.

Suppurative peritonitis must, therefore, be regarded from a practical standpoint as a circumscribed inflammation. The appearance and character of the pus are often greatly modified by the admixture of an extravasation accompanying the perforative lesion which produced the peritonitis. If the pus is thin, serous, we speak of a *sero-purulent peritonitis.* It is a serous peritonitis, with the formation of pus in sufficient quantity to render the serum more or less turbid. This subvariety of suppurative peritonitis is, without exception, in combination with fibrinous exudations which tend to limit the extension of the infective process. Sedimentation of the solid constituents takes place, so that the fluid contains more of the solid constituents in the most dependent portion of the affected district.

e. Serous Peritonitis. Independently of malignant and tubercular disease of the peritoneum, circumscribed hydrops of the peritoneal cavity is caused by a very mild form of peritonitis, the pus microbes present not being sufficient in quantity or virulence to produce pus. Patients usually recover rapidly from this form of peritonitis. The slight alterations of the peritoneum produced by the inflammatory process do not interfere with the transudation of serum, and resorption is effected as soon as inflammation subsides and the normal absorptive function of the peritoneum is restored. Serous peritonitis is usually more or less complicated by fibrinous peritonitis, as fragments of fibrin are often found suspended in the blood. The serum is generally somewhat turbid, not transparent, grayish-yellow or reddish in color. As long as the fluid is limited in quantity, it gravitates toward the most dependent parts of the abdominal cavity, in the small pelvis; when more copious, it reaches the upper portions of the peritoneal cavity and seeks first the depression on each side of the spinal column.

f. Fibrinoplastic Peritonitis. Peritonitis in which plastic exudations are formed and pus is absent or scanty, is called fibrinoplastic peritonitis. *Exudative peritonitis* and *peritonitis adhesiva seu sicca* have been used as synonymous terms for this variety of peritonitis. It is usually a secondary process, following a primary affection of one of the abdominal or pelvic organs, and denotes a mild form of infection, the extension of which becomes limited by firm adhesions. The inflammation results in a plastic exudation, with little or no effusion. The character of the exudate depends on the intensity and quality of the bacteriological cause. The exudation is often so copious that it has been mistaken for malignant disease. Goldberg reports two such cases. The symptoms were marked

cachexia, ascites, uncontrollable diarrhœa, and apparent tumor deep in the abdomen. The distinguishing features of this form of peritonitis from abdominal tumor are the less circumscribed outline, the lesser resistance offered, the more regular surface, and the fact that the ascitic fluid is not bloody, but serous or sero-purulent. The exudation, in the course of time, contracts and results in strong bands of adhesion which frequently flex and distort the organs to which they are attached, which has given rise to another term, *peritonitis deformans*.

4. BACTERIOLOGICAL CLASSIFICATION.

As the essential cause of peritonitis is always the presence and action of pathogenic microbes and their toxins upon the peritoneum, and as the character of the inflammatory process is largely influenced by the kind of microbes which produced the infection, a bacteriological classification is of the greatest scientific and practical importance. All pus microbes present in sufficient quantity and virulence in the peritoneal cavity can produce peritonitis. Experiments as well as clinical observations have shown, however, that their action is enhanced by local conditions which favor their growth and reproduction. Injuries or antecedent lesions of the peritoneum, and the presence of putrescible substances, furnish such predisposing and exciting conditions.

a. Streptococcus Infection. The streptococcus pyogenes is the microbe which is most frequently found in the tissues in cases of septic peritonitis. The infection spreads so rapidly over the peritoneal surface and through the subserous lymphatics that death, as a rule, occurs from septic intoxication before a sufficient length of time has elapsed for any gross pathological conditions to form. Absence of fibrinous exudate and effusion are the most striking negative findings at operations and necropsies. Streptococcus infection is the immediate cause of the most fatal form of puerperal peritonitis. Fränkel has found the streptococcus pyogenes in a great variety of puerperal diseases, especially in cases in which the local affection implicated the lymphatic vessels. In such cases, the microbes found entrance into the pelvic tissues from abrasions of the vagina or uterus, and by extension of the inflammatory process the broad ligaments and the peritoneum are successively reached. After the peritoneum has once been infected, rapid diffusion takes place, and finally the diaphragm and pleuræ are implicated in the same process, and the patient dies from the effects of progressive sepsis.

b. Staphylococcus Infection. In peritonitis caused by staphylococcus infection, the intrinsic tendency to localization of the disease is more marked; the inflammation results more often in circumscribed suppuration and limitation of the infective process by copious fibrinoplastic exudations. As a rule, the inflammation terminates in the formation of thick, cream-colored pus. Different forms of staphylococci are often seen in the same inflammatory product.

c. Pneumococcus Infection. It is now well known that pneumonia is produced by different microbes, but the diplococcus is found in about eighty per cent. of all cases. It is this microbe which occasionally is found as the bacteriological cause of acute suppurative peritonitis. Weichselbaum has found the diplococcus of pneumonia, unaccompanied by any other micro-organism in three cases of peritonitis. In one case the peritonitis and acute pneumonia occurred simultaneously; in the other double pleuritis followed the peritonitis, but in the last one the peritonitis was undoubtedly primary and, in the absence of any other microbes in the inflammatory product, must have been caused solely by the diplococcus of pneumonia.

Etheridge has described three cases of abscess of the ovary complicated by plastic peritonitis, in the contents of which the diplococcus alone was found. Le Gendre reports a case of peritonitis in a girl of eighteen; the pus was yellowish-green, lumpy, and of a fibrinous consistence, and contained a pure culture of the pneumococcus. The author found, altogether, eleven cases recorded, eight of which had been fatal. Another case is reported by Veillon. The suppuration caused by pneumococcus infection is almost invariably attended by copious fibrinoplastic exudation.

d. Bacillus Coli Commune Infection. The bacillus coli commune, a microbe that constantly infests the intestinal canal, is in a fair percentage of cases the bacteriological cause of acute peritonitis. This microbe possesses pyogenic properties, and in intestinal paresis and perforations escapes into the peritoneal cavity and produces usually a pathologically mixed form of peritonitis, that is, suppurative and fibrinoplastic peritonitis. In thirty-one cases of peritonitis examined by Fränkel, this microbe was found in nine. In eleven cases, seven gave mixed cultures, and in three of these the colon bacillus predominated. The same author has shown that pure cultures injected into the abdominal cavity of rabbits cause typical peritonitis.

c. Gonococcus Infection. In the peritoneal cavity the gonococcus produces a plastic peritonitis, and sometimes localized suppuration. Salpingo-peritonitis and more diffuse pelvic peritonitis is most frequently caused by gonococcus infection. "The proper character and results of the pathogenous activity of the gonorrhœic microbes are therefore seen, pure and unadulterated, in the tubes. They cause purulent inflammation of the mucous membrane, but the surrounding connective tissue remains free from them. The gonorrhœic tubal pus is evacuated into the peritoneum, and whereas in other conditions the bursting of an abscess into the abdominal cavity is followed by the gravest consequences, in this case the whole process terminates with a circumscribed inflammation, encapsuling the exuded pus. The cause of this difference is the varying pathogenic value of the organisms which are contained in the pus. A puerperal pelvic cellulitic abscess bursting into the peritoneum causes general peritonitis, because it contains pyogenic streptococci, which rapidly multiply in serous cavities and are capable of exerting the most deleterious effects. Gonorrhœal tubal pus cannot do this; its microbes do not find in the peritoneum conditions for their increase; the pus therefore acts as an aseptic foreign body, becomes encapsulated, and is finally absorbed (Sinclair).

f. Tubercular Infection. The rapid diffusion of the tubercle bacillus in the peritoneal cavity, either through the circulation or by rupture of a tubercular abscess into the peritoneal cavity, or by extension from a tubercular salpingitis, occasionally gives rise to a form of acute peritonitis, characterized as such in a modified way by the clinical manifestations which accompany it. According to the intensity of the infection or the degree of susceptibility of the patient to the action of the tubercle bacillus, the disease assumes one of the following pathological forms: 1, Tubercular ascites. 2, Fibrinoplastic peritonitis. 3, Adhesive peritonitis. Suppuration only takes place when the tubercular product becomes the seat of a secondary mixed infection with pus microbes.

5. CLINICAL CLASSIFICATION.

From a practical standpoint the clinical classification is the most important. A modern clinical classification must be based on the location, causes and pathological types of the inflammatory process as outlined above. Upon a correct clinical differentiation between

the various forms of peritonitis as seen at the bedside, depends largely the adoption of a rational course of treatment. The recognition of the disease no longer completes the diagnosis for the physician, and much less for the surgeon. A diagnosis for the careful physician and conscientious surgeon, must include the location, extent, causation and pathology of the disease. From the information obtained from the classification already made must be obtained the material upon which to base a clinical classification. Such a classification should serve as a guide in differentiating between the cases which demand surgical intervention and the cases which can be trusted to medical treatment.

a. Ecto-peritonitis. Abscess formation in the subperitoneal connective tissue, as seen most frequently in the pelvis in women, in the cavity of Retzius in men, and in the retroperitoneal space in both sexes, is always attended by inflammation of the outer surface of the peritoneum, and is not infrequently followed by extension of the infection through the lymphatic spaces to the free surface, and exposes the patients to the risks of perforation of the abscess into the free peritoneal cavity, septic diffuse peritonitis and death. Such abscesses should be recognized and accurately located sufficiently early to prevent such serious complications by an extra peritoneal incision and drainage; or, if the abscess is of a tubercular nature, by tapping, evacuation and iodoformization.

b. Diffuse Septic Peritonitis. This form of peritonitis is characterized clinically by the gravity of the general symptoms from the very incipiency of the disease; pathologically by the rapid diffusion of the infection over the entire serous surfaces, visceral and parietal; bacteriologically by the presence in most of the cases of the streptococcus pyogenes in the inflamed tissues. Staphylococci, pneumococci, and the colon bacillus may also be the cause of rapidly spreading diffuse peritonitis. This form of peritonitis usually follows penetrating wounds of the abdominal cavity, complicated by visceral injuries of the gastro-intestinal canal, contusion or laceration of any of the abdominal or pelvic organs, rupture of an abscess or ulcer into the free peritoneal cavity, or the extension of a septic lymphangitis from any of the abdominal or pelvic organs to the peritoneum. Strict aseptic precautions have succeeded in greatly reducing, but not entirely eliminating, the danger from this source in all operations requiring opening of the free peritoneal cavity. In genuine cases of diffuse septic peritonitis, surgical intervention is usually powerless in preventing speedy death from toxæmia.

c. Perforative Peritonitis. Perforative peritonitis invariably occurs as a secondary affection, usually in connection with an ulcerative or gangrenous lesion of any part of the gastro-intestinal canal. Perforative ulcer of the stomach, duodenum, or typhoid, or tubercular ulcers of the ileum, perforation or sloughing of the appendix, the different forms of intestinal obstruction, are the most frequent causes of this well-defined clinical form of peritonitis. Perforative peritonitis is manifested by the sudden onset of the disease, by diffuse pain and tenderness, rigid abdominal walls, fever, vomiting, the impossibility by inspection, palpation and auscultation to certain intestinal peristalsis, the latter being almost positive proof of the presence of gas in the free peritoneal cavity. According to the author's observations, meteorismus peritonei in perforative peritonitis caused by affections of the appendix is rare, while he has seldom found it absent in perforations of any other portion of the gastro-intestinal canal. According to the number and virulence of the microbes which find their way into the peritoneal cavity with the extravasation, the resulting peritonitis is either diffuse or more or less circumscribed. The colon bacillus is invaribly present in the inflammatory product, but in addition, streptococci, staphylococci, putrefactive bacilli, the typhoid bacillus, or bacillus of tuberculosis, according to the nature of the primary affection, may also be found.

Perforative peritonitis must be regarded and treated as a strictly surgical disease. The primary lesion must be exposed and treated as soon as a diagnosis can be made and the necessary measures applied to limit the extension of the infection and to prevent death from toxemia.

c. Circumscribed Peritonitis. A circumscribed peritonitis is an inflammation of the peritoneum, during which a greater or lesser part of the peritoneal cavity becomes excluded from the original source of infection by the formation of plastic visceral, parietal, or visceral and parietal adhesions. The complexus of symptoms varies according to the degree of virulence of the microbic cause, which only occasionally is overshadowed by the primary affection. The symptoms appear suddenly, or are preceded by those incident to the primary disease. The severity of the pain and the degree of the muscular rigidity and tenderness will correspond with the extent of the disease. The intensity of the general symptoms are determined more by the nature and virulence of the microbic cause than the size of the peritoneal surface involved. The inflammatory

focus may be limited to a very small space, or it may involve the greater portion of the peritoneal cavity and organs which it contains. The clinical course and termination are determined largely by the nature and virulence of the primary bacterial cause, the anatomical location of the primary starting point and nature of environment. If the organs adjacent to the primary focus of infection are favorably located to limitation of the process, diffusion is frequently prevented by the formation of adhesions. This is especially true in cases where the primary infection is limited by the existence of old adhesions. Localized peritonitis may be confined to the lesser peritoneum, particularly in cases of perforating ulcer of the stomach. More frequently it is caused by appendicitis and cæcitis. A very frequent cause of circumscribed peritonitis is inflammation about the gall bladder, uterus, Fallopian tubes and ovaries. The localized form of peritonitis is very often overlooked during life. It can usually only be detected if a demonstrable swelling forms at the seat of inflammation. The mildest form of infection gives rise to fibrinoplastic peritonitis, which leaves temporary or permanent adhesions, but terminates without pus formation. Circumscribed suppurative inflammation is always attended by fibrinoplastic peritonitis, the products of which and the viscera which it involves form the abscess wall. The microbes which produce most frequently fibrinoplastic peritonitis without suppuration are the gonococcus and the staphylococci. Circumscribed suppurative peritonitis is usually the result of infection with staphylococci, bacillus coli commune and pneumococci. In fibrinoplastic peritonitis surgical interference becomes only necessary when intestinal obstruction is caused by the adhesions. In circumscribed suppurative peritonitis the pus should be evacuated as soon as the disease is recognized, and if possible by an extraperitoneal route.

d. Hæmatogenous Peritonitis. In very rare instances peritonitis occurs without any injury or discoverable antecedent lesion of any of the abdominal or pelvic organs, and is then described as idiopathic peritonitis. As peritonitis is always caused by bacteria of some kind, a peritonitis that develops independently of a local source of infection is the result of an infection through the blood, and should be called hæmatogenous or metastatic peritonitis. It has been observed in connection with nephritis, pyæmia, rheumatic arthritis, and acute exanthematous diseases.

e. Visceral Peritonitis. A localized peritonitis that can be brought in direct etiological connection with the organ primarily affected

is expressed by a compound word with the prefix *peri* and the noun used to indicate the organ primarily affected in a state of inflammation. Thus the anatomical forms of peritonitis present themselves:

Perigastritis,
Perienteritis,
Perityphlitis,
Periappendicitis,
Pericolitis,
Perihepatitis,
Perisplenitis,
Pericystitis (urinary and gall bladder),
Perimetritis,
Perisalpingitis, and
Perioöphoritis.

As the mesentery and omentum are only duplications of the peritoneum, we have to add to the above anatomical forms mesenteritis and epiploitis.

f. Pelvic Peritonitis. Pelvic peritonitis is seldom met with in the male. It is a form of peritonitis in which the female pelvic organs are the primary starting-point of infection, with extension to the peritoneum, either through the Fallopian tubes, or the lymphatics of the uterus or its adnexa. It is caused most frequently by gonorrhœal or puerperal infection, or develops after instrumental examination of the interior of the uterus or operations upon this organ.

g. Puerperal Peritonitis. By the term puerperal peritonitis is understood a progressive inflammation of the peritoneum, occurring in consequence of an extension of an infection from any part of the genital tract in puerperal women after delivery or abortion. The infection usually takes place through the lymphatics, which in the majority of cases terminates in diffuse septic peritonitis.

h. Subdiaphragmatic Peritonitis. A peritonitis limited to the under surface of the diaphragm and any of the adjacent organs is called subdiaphragmatic peritonitis. If the inflammation remains limited and life is sufficiently prolonged, it usually terminates in the formation of a subdiaphragmatic abscess.

SYNOPSIS OF CLASSIFICATION OF ACUTE PERITONITIS.

Anatomical.

- Ecto-peritonitis,
- Endo-peritonitis,
- Parietal "
- Visceral "
- Mesenteritis,
- Epiploitis,
- Perigastritis,
- Perienteritis,
- Perityphlitis,
- Periappendicitis,
- Pericolitis,
- Perihepatitis,
- Perisplenitis,
- Pericystitis (urinary and gall bladder),
- Perimetritis,
- Perisalpingitis,
- Perioöphoritis,
- Pelvic peritonitis,
- Diaphragmatic peritonitis.

Etiological.

- Traumatic peritonitis,
- Idiopathic "
- Perforative "
- Metastatic "
- Puerperal "
- Peritonitis infantum,
- Fœtal and intrauterine peritonitis,
- Peritonitis neonatorum.

Pathological.

- Diffuse septic peritonitis,
- Putrid peritonitis,
- Hemorrhagic "
- Suppurative "
- Serous "
- Fibrinoplastic peritonitis.

Bacteriological.

- Streptococcus infection,
- Staphylococcus "
- Pneumococcus "
- Bacillus Coli commune infection,
- Gonococcus infection,
- Tubercular "

- Clinical.
  - Ectoperitonitis,
  - Diffuse septic peritonitis.
  - Perforative "
  - Circumscribed "
  - Hæmatogenous "
  - Visceral peritonitis.
    - Mesenteritis,
    - Epiploitis,
    - Perigastritis,
    - Perienteritis,
    - Perityphlitis,
    - Periappendicitis,
    - Pericolitis,
    - Perihepatitis,
    - Perisplenitis,
    - Pericystitis,
    - Perimetritis,
    - Perisalpingitis,
    - Perioöphoritis.
  - Pelvic peritonitis,
  - Puerperal "
  - Subdiaphragmatic.

ACUTE GENERAL PERITONITIS.

The Prognosis and Treatment.

BY ROBERT ABBÉ, M.D.

of New York.

Twenty years ago, the dread of peritonitis after operations within the abdominal cavity, where previous inflammation did not exist, was still the bugbear of surgery. It has gradually occupied a lessening position of seriousness in the calculations of the operator, until to-day the surgeon, who is properly cognizant of the powers of the peritoneum to aid him when respectfully treated, completes his work (no matter what immediate soiling has occurred, be it extravasation of bile, urine, feces, or pus), with slight apprehension that post-operative peritonitis will occur. The once-dreaded invasion of the peritoneal cavity has become a matter of safe conduct when the operator is the invader. Nevertheless, this same cavity has become a battleground of great interest in the surgical field to-day, when, not the surgeon, but germ-laden matter, is the invader, and precedes the surgeon by many hours. Here the race becomes unequal. A death-dealing blow has been dealt to the human body in one of its most vital parts; a blow from which it is possible to rally, under some circumstances, by intrinsic powers of resistance, but which, under most conditions, is followed by an encounter, the outcome of which will often depend on extrinsic aid from the physician and surgeon.

It is to the study of this most important and narrowing field that our attention is turned.

That the peritoneal cavity is not equally impregnable in all its parts is a well-established fact. Not that the same susceptibility does not exist in all anatomically similar portions of its surface, but, from varying contour, or proximity to actively moving viscera, it transpires that the greater part of those invasions which originate in the pelvis, or in the fossæ outside the colon, or in a less measure in the area anterior to the stomach and liver and above the colon, become localized within a few hours, and are under the control of Nature's reparative processes in the confines of quickly built-up

lymph walls; while a discharge of offending secretions into the central part, among the small intestines, becomes a grave menace, from causes, the principal of which seems to be the difficulty encountered in throwing up barriers in the presence of quick-moving intestinal coils, which rapidly distribute the infection.

Hence, we shall see that the location of the invasion, independent of the quantity and virulence of the material spread about, has much to do with determining the gravity of the case and the need of action. The scholarly treatment of the subject of general peritonitis, in all its minor and major phases, by Treves and other writers, and the graphic delineation by Dr. Senn of the varieties and classification, impress upon our minds the value of thorough understanding of the nature of peritonitis and the methods adopted by Nature to save life. They prepare us to accept the dictum that all peritoneal invasions by infectious processes, of which we shall speak, are essentially fraught with the greatest peril. Although general peritonitis may originate in any portion of the cavity, we must exclude from our thoughts in this discussion all limited forms, no matter how grave their concomitant symptoms. We know that an intra-abdominal abscess or slight infection may be accompanied by so grave symptoms that, to the clinician, it may seem to be a case of general peritonitis, and a surgeon may even wrongly report operation on general peritonitis, because he has opened an enormous abdominal abscess which had crowded the uninflamed intestines into the upper part of the abdomen.

The grave form of acute general peritonitis which we are to consider is one which is caused almost universally by the rupture of some one of the hollow viscera (stomach, intestines, appendix, or bladder), and for the practical surgeon need not be classified on any but a clinical basis. We must accept the universal bacterial origin of peritonitis, and regard the victim as poisoned by the septicæmic infection. Apart from all other considerations, we must say that "acute general peritonitis" shall include only those cases in which infection is not confined by any lymph barriers. The stage at which it is seen will determine the area of the peritoneum invaded. The affection is the same whether it include half or all of the entire peritoneum—for who can say when the last few inches are affected? The case which we operate on to-day and find universal, had spread to only half the abdomen yesterday, and six hours earlier to one-quarter of its area. The surgeon has to form an estimate of each particular case, at the time of operation, by the

naked-eye appearances, and thus classify it as to gravity. If he has been fortunate enough to inspect it by early operation, he will find most various appearances, all illustrating an early stage of a disease inevitably advancing to a fatal issue. The one essential feature that allows a case to be classed as acute general peritonitis is that there are no boundary limits. Given a turbid, semi-purulent or purulent effusion about inflamed small intestines, arising from perforated stomach or gangrenous appendix, with no effort of Nature to wall it in, and the fatal end of the case is not far off, unless arrested by the surgeon. Septic affection has already occurred, and Nature has failed to wall it in.

The only subclassification of this form of peritonitis is into the early and late stage. Both are equally grave if left to Nature.

Opinion has been growing sceptical as to the value of operation in this form of peritonitis in any stage. Speaking of general diffused non-tuberculous peritonitis, Treves says: "I am doubtful if a single human life has been saved by surgical interference in a genuine case of peritoneal toxemia." Richardson says: "In a large number of cases of general peritonitis, verified by bacteriologic examination, the result with hardly an exception has been fatal in my hands under any method of treatment." Weir says that he had never been able to save a patient, nor had he seen one saved. Von Winivarter, after a large experience, writes: "In not a single case where the exudate had a fecal odor have I succeeded in saving my patients, all have succumbed to the septic intoxication. . . . We possess no means of checking a peritonitis of septic character." Regnier says: "Laparotomy and lavage are unavailing for the cure of a true general peritonitis. The various cases we hear of are cases of large encysted purulent collections." Delorme says: "I have operated on many cases of peritonitis, and I have lost all my patients."

Facing this pessimistic opinion, which is echoed from many sources, it seems evident that the optimism of those who report from thirty to sixty per cent. of cures, is born of a misunderstanding of the variety of the disease discussed. Let us then make no mistake in appreciating the character of the disease.

As I have already stated, the only warrant for classing cases under this head is the presence of reasonably extensive involvement of some part of the small intestine from foul contamination, which is absolutely not limited by any boundary adhesions. As far as septicæmia goes, they are all septic, and that, under the above conditions, is practically a guarantee of the ultimate fatal issue,

under expectant treatment. Demonstration of the presence of noxious bacteria in the exudation has been so constantly shown that it may be admitted to be universal. Acute general peritonitis is an *a priori* argument of their existence.

The variety of the bacterial flora corresponds with that found within the intestines. Elaborate research has already demonstrated the streptococcus and bacillus coli commune as most uniformly present. Therefore, we are prepared to study the prognosis of *unlimited peritonitis* from an operative point of view, regarding it, if fairly widely developed, as being on the high road to a fatal issue.

The effort made by the system of the patient to protect and rid itself of the parasitic assault, is a complicated and beautiful one. The power of the peritoneum to rapidly remove large quantities of fluid, introduced experimentally in animals, as studied by Wegner and others, demonstrates that from three to eight per cent. of the animal's weight of fluid can be taken up in an hour—equivalent to the entire weight in one day. Muscatello demonstrated, also, (*Virchow's Archives*, 1895) that the current of absorption is toward the diaphragm, which fact is of practical import. Carmine particles suspended in fluid are quickly carried through the intercellular openings in the peritoneum covering the diaphragm, into lymph spaces beneath, where direct communication is had with the mediastinal glands. Here the parasites can be found arrested in five to seven minutes' time if the animal is held head downward.

Before the visceral peritoneum begins absorption into the lymphatic system of the mesentery, that which lines the diaphragm has given exit to bacterial infection and leucocytes, which are speedily taken into the blood current and sent to the large abdominal organs —the liver, spleen, and kidneys.

Experimental research shows that when a small amount of infectious culture of intestinal bacteria is injected (a cloudy emulsion of 5 or 10 c.c.) it can be disposed of without fatal effect. A small quantity produces diarrhœa; more, a local peritonitis; still more, a fatal fibropurulent peritonitis—and a larger dose, acute fatal sepsis, without peritonitis. Examination of the survivors shows no streptococci in the peritoneum 5½ hours after injection of small quantities. The experiments of Barron and others, however, show that a very minute quantity of fluid from an inflamed part (such as fluid from puerperal peritonitis) produces much graver symptoms than a larger quantity of a culture from the same germ. The destruction of bacteria by phagocytosis, and the unexplained bac-

tericidal action of blood-serum, are coincident methods called into action in the emergency and need no description here. When the infection is severe they are inadequate, and every organ teems with bacteria soon after pronounced septicæmic symptoms appear.

With such recognition of the power of the peritoneum to rid itself of small toxic doses, we turn to the demands made upon it by disease and accident. Taking the experience of hospital surgery as representing an average, we find that acute general peritonitis results, in the majority of cases, from infection starting from the appendix; second to that, perforating gastric ulcers, intestinal traumatisms, ruptured pelvic abscesses. Ruptured urinary and gall-bladders occupy a relatively smaller place.

With the nature of the invading medium, it is evident, the virulence of the attack must vary. A discharge of stomach secretion into the peritoneum seems not to be so quickly toxic as a minute quantity of active poison pent up in an already inflamed appendix, yet the former by its eroding action on the endothelium paves the way for absorption soon after. So also with normal urine or intestinal contents not in a state of inflammatory ferment at the time of invasion. In such cases septicæmic symptoms supervene some hours after the accident. Perforating gastric ulcer, if it has time to leak slowly into the peritoneum, will almost surely be controlled by adhesions, and the alert operator may save general invasion by incising the epigastric abscess.

Most perforations, however, occur after a meal, and general peritonitis is set up simultaneously from the stomach to the pelvis. The degree of inflammation found will be in exact ratio to the lapse of time before operation.

Recent statistics show that, up to five years since, no operative case for perforating gastric or duodenal ulcer had recovered. Weir has recently collected 97 operations, with 22 recoveries, and to his statistics I am able to add a summary of twenty reported later, three of these being my own. In these additional 20, general peritoneal extravasation occurred in 18, and of this number 12 recovered and 6 died. Out of the 12 recoveries, operation was performed within ten hours in 7 and after twenty-four hours in 5, showing the value of prompt action. Of the six fatal cases, in all but one operation had been delayed until after the first day. In two fatal cases the peritonitis was practically cured, but the patients succumbed to septic pneumonia as late as the seventeenth and twentieth days. Weir says, in reviewing his statistics: "More than half of all the

patients operated on in the first twelve hours recovered, the mortality being 39 per cent.; while of those operated on from twelve to twenty-four hours after perforation, 70 per cent. died, and of those who came to operation after the first day, 87 per cent. succumbed." In conclusion, he says: "The happy result of operation is dependent more upon its early performance than upon any other factor." My own feeling is most hopeful that future contributions to this subject will show that the earlier we can operate on these cases, the more surely will we be able to combat the disastrous accident.

In gunshot, or stab, or penetrating wounds of the abdomen, there is a universal concensus of opinion that operation at the earliest possible moment is the only justifiable attitude. The surgeon can never be absolutely positive some organ is not injured, or that there exists concealed extravasation, until he has seen the invaded part. If it be a slight stab wound, or if shock is greater than will warrant anesthesia, it is incumbent on the surgeon to make an incision or an extension of the wound under cocaine anesthesia, and if nothing be discovered he may then be justified, and only then, in awaiting symptoms. If he finds perforation or hemorrhage, a temporary arrest of the flow will be conservative until two or three hours have given the patient time to recover from shock. The statistics of gunshot wounds corroborate the value of promptness, as seen in every other case of abdominal work. Of 39 cases operated on within twelve hours, 18 recovered, while of 22 after twelve hours, only 5 recovered. Likewise in rupture of the urinary bladder, which was uniformly a fatal accident until recently, the mortality has been reduced from 90 to 50 per cent. during fifteen years. Sieur's paper reports 34 cases and 14 recoveries. Schlanger notes 22 operations and 10 recoveries. The evidence is accumulating that early cleansing and draining will insure a prompt recovery, unless cystitis be previously present when the chance of grave peritonitis is enhanced. So also if the gall-bladder be inflamed at the time of injury, the bile is swarming with bacteria, notably the coli commune, which have worked back from the duodenum, and septic peritonitis is imminent unless quick and thorough precaution be taken. Normal bile, however, will be fairly well borne and disposed of by the uninflamed peritoneum.

The phase of acute general peritonitis from perforating typhoid ulcer has seemed to me to differ but little in its course and treatment from that following ulceration of other parts of the alimentary canal. The patient's lower vitality does not militate so greatly against

recovery as one would imagine. The peritoneum is able to throw reparative lymph about a slow perforation, though usually it is overwhelmed by a sudden liquid extravasation. The beneficial results of interference are shown by the case of Van Hook, which, as yet, stands unequalled. He operated at two in the afternoon in a case where rupture occurred at five in the morning (nine hours before). Extravasation had taken place wide of the ulcer. The opening was sutured, the abdominal cavity thoroughly washed out, and the patient rescued from collapse, and saved. Excluding all doubtful cases, Finney finds 11 recoveries after 45 operations, showing a success in 26 per cent.—certainly a very admirable showing in the face of practically certain death. The evidence, as he shows, is clearly in favor of early operation. The most striking recoveries were among those operated upon within twelve hours after the accident.

It is well recognized that in this trouble there is a marked signal symptom of the beginning of perforation. The patient has "sharp continued abdominal pain coupled with nausea." As in gastric perforation, the patient feels, as I have heard it expressed, either a "tearing pain," or as if something had given away. Hence, the attending physician has, in most cases, every reason to suspect the nature of the disaster, and little excuse for masking the symptom by morphine while waiting for peritonitis to set in before surgical aid.

After the foregoing considerations, we are now able more intelligently to consider the prognosis in that disastrous condition, seemingly more common every day, viz., acute general peritonitis of appendical origin. Granted that ninety per cent. or ninety-five per cent. of mild attacks of appendicitis pass over without grave results, there still falls to the lot of the surgeon that unhappy group of septic cases which are presented to him for cure by the too often delinquent practitioner, after from two to five days of hopeless expectancy. Of this type, with non-limited inflammation, all are in various stages of septicæmia, and the dullest observer must admit that be it early or late, the patient is on the highway to more profound infection and inevitable death. The literature of the last two or three years teems with references to individual cases and opinions, showing confusion of classification and reporting oftentimes doubtful cases.

I have chosen therefore to ask you to consider a very few reported consecutive cases representative of this class.

Two years since McBurney chose a group of twenty-four cases distinctively of this type operated on by himself during the previous five years and gave brief details of each, sufficient to identify it as justly classified. He also regards general peritonitis as including those not only which are seemingly universal, but such as involve half or a quarter of the intestinal surface and are spreading without barrier at the time of operation. Of his twenty-four cases he saved fourteen. One reads, though, that in some cases, limiting barriers had been thrown up, but had subsequently burst and scattered the pus far in advance, among the coils of intestine. McCosh, also, in a paper recently read before the Surgical Society, chose, among his hospital cases, eight during the past two years and forty-three during the previous seven, which he had submitted to radical operation. Of the forty-three in the earlier group thirty-seven died (86 per cent.). Of the eight during the past two years two died. Of all the fifty-one cases thirty-nine died (or 76 per cent.). He has carefully confined his choice to cases of distinctly generalized peritonitis.

In my own practice I have chosen, with the same point in view, thirty-three cases, all that I have operated on during the past five years from among several hundred laparotomies. I would also add ten well-observed cases ably reported by Lockwood (*L. Clin. Jour.*, April 1, 1896) and nineteen consecutive cases during two years by Koerte (*Berlin. Kl. Woch.*, Aug., 1892). It would be unnecessary to enlarge this list for present discussion, and we may fairly say that this group of 137 cases are representative, and would be duplicated in consecutive work by most operating surgeons. As already remarked, it is only fair to the discussion to divide these into two groups, representing an early stage and a late stage as nearly as possible. A picture of the two types would be represented by what may be presumed to be the condition of the same patient operated on at the end of twelve hours or neglected until the third day.

From the mild type are excluded all those cases where clear serous effusion is found free, and from the grave type those where pus is scattered from an abscess at operation, or just prior to it, even though it be found smearing the intestines beyond confines.

In the first picture, the early stages, a day or two after a sharp onset of symptoms, operation will release turbulent or semi-purulent fluid, which will flow from between presenting coils of intestine before the appendix is reached, and will uniformly be found in

considerable quantity in the lower pelvic pouch. When the operator has dried all presenting parts, he draws the dusky, inflamed intestines toward him, and finds no barriers of lymph adhesion; but as he sponges between the coils and advances into the center of the small intestine area, there is less and less appearance of inflammation. When the visible evidences are less, he thrusts sterile gauze pads still further into the interintestinal spaces, and later, on withdrawing them, finds them wet with clearer effusion than that already removed. He rests satisfied. The appendix in these cases may be either slightly perforated or gangrenous, free among the intestinal coils, or hanging loosely in the pelvis. It is bathed in foul-looking fluid, more turbid than appears elsewhere, and usually has a slimy, virulent-looking coating of non-adhesive exudation. If not thinned by gangrene of its coats, it is highly inflamed and hard.

If treated expectantly it will represent the second class in from one to three days, and on incision thin pus (usually offensive) will stream out of the operative wound—will be found floating the bowels out of the pelvis, and come equally from the opposite side of the abdomen, or in the median line above the navel. The intestines are thickened or even granular, and reddened lymph patches are loosely and irregularly adherent. It is no wonder that surgeons stand appalled before this class and are sceptical as to their ever being cured.

Taking the reports mentioned as the most fair that I can find for study, we have the following showing:

McBurney, 24 cases, 16 recoveries; McCosh, 50 cases, 12 recoveries; Abbe, 33 cases, 9 recoveries; Lockwood, 10 cases, 3 recoveries; Koerte, 19 cases, 6 recoveries. Total—137 cases; 46 recoveries. It is possible in many of these to divide them into the two classes previously mentioned.

In my own, of which I have clear records, I can assert that of the 33 cases, 6 were of the milder type, but progressing rapidly, when operated upon, and 27 were of the grave type. Of the mild type 5 were operated on early, and 1 on the fifth day—all recovered. Of the grave 11 were operated on within two days, 3 recovered, 8 died; 16 were operated on from two to five days after the attack—all died.

Of the reported cases of McBurney and McCosh it is not easy to thus classify many of them, but choosing 28 cases, in which the time of operation is indicated, there were 18 of the grave type, and

10 of the milder. Of 6 grave cases taken within 1½ days, 4 recovered, 2 died; of 8 grave cases taken within 2½ days, 4 recovered, 4 died; of 4 grave cases taken within 2½ days, all died. Of 10 cases of milder type, 3 cases taken within 1½ days, all recovered; 2 cases within 2½ days, all recovered; 5 cases after 2½ days, 1 died. Of 19 cases of Koerte, 16 operated within 4 days,, 6 recoveries; 3 over 4 days, all died.

For a summary then, we may say that choosing only those 16 which are certainly of the milder type, judging from personal knowledge or the records, only 1 died. Of the graver type, 64; where the time is noted, the 17 recoveries were all obtained inside of 2½ days. There is but one logical deduction from this review—and that corresponds with the same drawn with regard to perforations of the stomach and intestines—namely, that the element of time is the one of greatest importance. The earlier the operation the greater the hope. Only 1 death occurred in 16 slighter forms of advancing general infection, and almost no case of the graver type recovered after 2½ days from the hour of attack, the earlier periods showing most recoveries.

There is one point I have discovered in the review, that, of numerous cases where recovery takes place, albumin or casts are not found in the urine. I ask careful consideration of this by future reporters, because it would seem that where the kidneys are choked up by the bacteria of septicæmia it is practically useless to operate.

If time permitted, I would gladly give some thought to the evidences which distinguish a true case of beginning dangerous peritonitis from the milder local troubles which often begin with seemingly the same violence.

Are there any entirely characteristic symptoms?

A study of the initial signs, in cases which have come to operation and had been proved, has shown me that uniformity of symptoms is entirely wanting. A persistent diffused tenderness spreading to the opposite side of the abdomen is very grave. A board-like stiffness of both sides of the abdomen is suggestive. Tenderness at a point in the rectum as high as the finger can reach in the median line, is a sure index of either an inflamed appendix hanging over the pelvic brim, or an acute peritonitis. A pulse that is rapid and quick, or "snappy," is almost a sure index of septic toxemia, and, if it persists more than twelve hours, calls for interference.

Vomiting will usually occur once with most mild attacks, but if persistent indicates mischief. The tongue may be clean and moist

and the eye bright in one-third of the cases of grave peritonitis, even after two or three days.

The facies of abdominal inflammation is more often a late symptom.

Thoracic respiration is very often seen when spreading peritonitis prevails.

The temperature is frequently but little elevated during the first day or two, while the pulse may be showing great agitation.

These danger signals may serve to aid diagnosis before profound toxemia sets in; when the surgeon can do nothing.

Regarding treatment, substantial progress has been made in determining the lines of action.

There is but one opinion regarding the cleansing of the abdominal cavity when only the lower segment has, as yet, been invaded. The moment the surgeon sees septic fluid, he sponges it away before it can be scattered. He mops the presenting bowels with sponges in clamps, dripping wet with hot salt solution (℥ iss to a quart), and dries them again before drawing other coils into the field of inspection. As soon as parts are found not much inflamed, he pushes a sterilized gauze tamponade, properly folded, among the bowels far away from the field of work. This has a tape sewed to it, to which a clamp is fixed and left outside the wound. One or two such tamponades may be thrust upward and across the abdomen before the pelvis is cleansed, to which much attention is *always* to be given. This being thoroughly mopped out, a light packing of mild iodoform gauze is to be placed in the pelvis, and a short way among intestinal coils elsewhere, especially if the gauze tamponades now removed prove to have come out wet, absorbing the thin effusion from a distance. The abdominal wound should never be closed in any septic case. It wastes time, confines infection, and prevents drainage.

In the grave cases, a long median incision, or two lateral ones, will always be needed. The lumbar drainage incision will only be necessary when the median cut is used alone.

The question of drainage has been thoroughly settled in favor of ample gauze packing as against rubber or glass tubes.

The lymph barrier, quickly thrown out by the peritoneum wherever the gauze is in contact, at once forms a boundary line, beyond which one process is going on, namely, absorption, destruction, and elimination of the marginal infection, already entrapped, while at the site of packing the current is reversed and everything is sucked into the gauze and removed.

When infection has been widespread, there is but one alternative —irrigation. By flushing the interintestinal spaces systematically with hot salt water, as hot as the operator's hand can bear (which will be over 105°, usually), these effects are produced. The water cleanses and stimulates the patient amazingly. One sees the pulse respond at once and remain steady long after the operation, and the absorbing power of the washed endothelium is diminished. This has been shown by experiments of Kinscherf on animals, where doses of strychnine or bichloride of mercury left after irrigation were not absorbed, while the same put into the peritoneum of dogs not irrigated were fatal. Thus the toxine absorption is temporarily arrested, while the patient fights for time to discharge the burden already taken up.

In the large abdominal incisions in bad cases, it is wise to leave the wound widely open; the gauze will hold back the intestines, and abdominal straps and binder will support the abdominal walls.

If the intestines are distended with gas and fluid feces, it is well to let them come out of the abdomen, receive them on hot towels in charge of an assistant, and prick one or two prominent places with a knife to evacuate gas and noxious excreta, which is washed away with a constant hot stream. Through one opening there should then be injected a syringe full of saturated solution of Epsom salts and the puncture closed. I have done this on three occasions during the past three years, but only in the very worst cases.

McCosh, however, advises in all bad cases to pass such a dose of salts through an aspirating needle into the bowel and close the aperture with one suture, which I heartily endorse as a routine procedure. It cannot be vomited, it excites downward peristalsis, and as it aids to carry off impurities, it proves of the greatest value.

In regurgitation, lavage of the stomach should be done before and after operation, and repeated as soon as regurgitation is renewed.

The rectal tube to relieve distention by gas is of inestimable value, and its use not infrequently marks the turning point in the disease by promoting downward peristalsis.

Some of the most brilliant recoveries I have had have been where the attending doctor has been ineffectually plying the patient with calomel or physic, which acted only after operation, or where a good dose of calomel taken after operation has rid the body of all noxious excretions on the second or third day.

The value of an ice coil, or light broad ice bags, after a general peritonitis, cannot be overlooked. I have great faith in cold thus

used to retard the inflammatory action and bacterial growth, either before or after operation. Moreover, it is almost uniformly grateful to the patient.

I will not detail other restorative measures which must be applied on general principles. Strychnia, 1-40 gr. every two hours, is sometimes necessary, and in cases of severe pain when the patient is well out of ether, morphine, hypodermically, is rather helpful than otherwise.

In conclusion, I would say that close study of the bad cases of general peritonitis shows it to be one of the most absolutely fatal maladies with which we have to deal. It has also been demonstrated that logically and statistically the earlier the operation on the lines delineated the better the prognosis. It has been further shown that even in the bad form, if operation be done and a masterly irrigation be carried out there still remains a chance for life, if the period elapsing be not more than two and one-half days. In cases where albumen and casts show in the urine, it is proof enough that the system is already overwhelmed and the kidneys and other glands are choked and the operation hopeless.

The burden of responsibility, then, for fatal issues in so many cases lies not with the surgeon so much as with those who withhold from him the opportunity to render the prompt aid which we have shown is the only chance. The ideal success may be accomplished in the future not more by new methods than by new opportunities. The ideal operation may be, the old method under ideal circumstances as to time.

Paper in Discussion,

by Dr. Andrew J. McCosh, New York.

We have listened to a very able paper on the classification of the different forms of peritonitis. I think that some of us were in hopes, however, that the classification could have been more practical and less elaborate, but such a classification is not possible apparently at the present day, if Dr. Senn is unable to formulate it. In regard to his pathological divisions, it seems to me that it must be difficult, at the time of operation, to distinguish between the three forms, diffuse septic, putrid and general suppurative peritonitis. These forms frequently intermingle, so that it is often difficult to tell where one begins and the other ends.

I did not know that the discussion of the treatment was to fall so largely upon me, so that I shall say but little concerning the prognosis, except that I thoroughly believe with Dr. Abbe that the duration of the disease has the greatest influence upon its outcome. I believe there is another factor besides the virulence of the disease, and that is the varying resisting power of different patients. Age and habits seem also to be factors of importance. We know that patients with a crippled liver or diseased kidneys are very susceptible to peritoneal sepsis. Most of my patients that have recovered from diffuse septic peritonitis have been under 35 years of age; I do not remember a single case above 45 that has recovered.

In regard to the treatment, I agree with almost everything that Dr. Abbe has said. It seems to me, however, that it is somewhat difficult, at the time of the operation, to divide the cases into two classes, namely: those that need mere cleansing with gauze or sponges, and those that need irrigation. We know that often in the most virulent cases the evidences of septic inflammation are but little marked, whereas in the milder cases the evidences are sometimes much more decided. I am now speaking solely of diffuse septic peritonitis. It seems to me that, at the time of operation, we should consider every case as of the severest type, and so treat it. Therefore, if irrigation is the most effectual means of cleansing the peritoneal cavity, we ought to adopt it in preference to sponging. I think that irrigation is not only a better means of cleansing, but that it also does less damage to the peritoneal endothelium than does the scrubbing process, which I think must injure its vitality, lessen its power of resistance against infection and encourage the migration of the colon bacilli through the wall of the intestine. I thoroughly agree with Dr. Abbe in regard to the importance of complete irrigation. It is my custom, after making a free incision, to turn the patient on the side and allow the intestines to escape. In former years I was doubtful about the propriety of this procedure, on account of shock and the possible inability to return the coils. In later years, however, I have become convinced of the value of this procedure, and in my opinion it adds but little to the shock of the operation, provided, however, that the intestines and the peritoneal surfaces are kept warm. The coils should be received into hot towels held in the hands of an assistant. While in this position outside the abdominal cavity, flaskful after flaskful of hot salt solution is poured over and through them, and at the same time a rubber hose is pouring the same solution into all the corners and crevices of the peritoneal cav-

ity. The irrigating fluid should have a temperature of at least 110°. I think it is now generally accepted that salt solution should be employed. Various other solutions have been tried, bichloride of mercury, carbolic acid, boracic acid, etc., but most of the surgeons now agree that normal salt solution is the safest and best. It is of considerable importance to allow a certain amount of this fluid to remain behind in the abdominal cavity. It acts as a needed heart-stimulant, increases intestinal drainage and encourages the septic current to flow out of the peritoneal cavity into the intestine. It has been shown that the injection of sterile fluids into the peritoneal cavity of animals increases their resistance to infection. Of course, as has already been stated, we do not claim that the peritoneal cavity can be thoroughly cleaned, by irrigation or by any other method. It is important, however, to remove as much of this septic material as possible, and to dilute what remains by a sterile fluid.

Another point of importance is in regard to the respective advantages and disadvantages of opium and cathartics. I have noticed in recent papers that there is an inclination to advise the use of opium in full doses and to discourage the use of catharsis. I am entirely opposed to this and feel that opium is the very worst treatment we can adopt in cases of general septic peritonitis. Of course in cases of so-called plastic or idiopathic peritonitis it is indicated; also in cases where it may be possible to confine the septic process to a comparatively small area.

What we most fear is intestinal paralysis, and every method should be employed to prevent this and to restore to the intestines their normal peristaltic action. Every means should be employed to encourage intestinal drainage, to prevent the distension and thinning of the walls of the gut, the stagnation of blood, all of which conditions favor the emigration of the colon bacillus out of the intestinal into the peritoneal cavity. The hopelessness of these cases often seems to me to depend on the inability to retain cathartics. On this account, some years ago, I began to administer intraintestinal injections of various cathartic drugs. At first I was discouraged, but in the past year or two I have become convinced of the value of this procedure, and I now employ in nearly every case of general septic peritonitis the injection of one or two ounces of magnesium sulphate. The injection is made with a syringe and aspirating needle into the jejunum or ileum at as high a point as possible. Since the adoption of this treatment my results have been so much better than those of preceding years, that I am

led to believe that they have been considerably influenced by the employment of the injection of the saline cathartic.

I dislike exceedingly to refer to my personal results, but as Dr. Abbe has already in the most flattering manner referred to them, and as I have laid so much stress upon the importance of saline injections, I beg leave to say a word concerning my statistics. Between 1887 and 1895 my mortality in 43 cases of diffuse septic peritonitis was about 87%. Between January 1896 and the present time I have operated upon nine such cases, six of which have recovered and three have died. These results were perhaps largely due to a fortunate coincidence in encountering so many patients of young age and vigorous condition, but I cannot help but feel that the use of saline cathartics had considerable influence on these results. These cases did not seem milder than those encountered in former years. With one exception the peritonitis had begun 20 hours, or longer, before the operation was done. In one there was a perforating gastric ulcer, in one a fetid ovarian abscess, and in seven a gangrenous appendix. We all feel, I think, that when the patient's bowels have moved that the point of greatest danger has passed, and in this connection it may be of interest to state that in the cases which recovered, in three the bowels moved within 24 hours, in two within 36 hours and in one only as late as 48 hours. Some of these cases, at the time of operation, seemed so hopeless that an absolutely bad prognosis was given by myself and others. From past experience, it seemed to me that in those cases where the distension was very great, and where vomiting was constant, that the tympanitis would increase, that the vomiting would persist, that the constipation would be absolute, and that death must occur on the second or third day. Much to my surprise, in several of these cases improvement began within 24 hours, flatus being expelled and a movement of the bowels following soon afterwards.

In regard to the effect of cold on the abdominal wall as a means of limiting bacterial growth inside the peritoneal cavity, I do not feel that we can place much value on this method. The experiments of Gilman Thompson and others have shown how little, if any, influence is exerted on intra-abdominal temperature by either heat or cold applied externally. Cold, however, is a comfort to the patient; it whips up the local circulation and possibly encourages intestinal peristalsis.

Drainage is of the greatest importance in these cases. The preference with most surgeons is for the insertion of gauze strips running in different directions among the intestinal coils. Some-

times glass tubes are useful; rubber tubes are less effectual. Recently I have been using strips of silk pongee, which seem to drain as well as gauze and are easier to remove. I think that chloroform is the best anæsthetic. I am in the habit of administering, immediately after the operation, 10 grains of calomel which will often be retained, at least if chloroform has been used. In conclusion, I would say that success depends on early operation, thorough cleansing, efficient drainage and ability to restore intestinal peristalsis.

Paper by Dr. George Ryerson Fowler, Brooklyn, N. Y.

Classification. For the purposes of the practical surgeon a good working classification of septic peritonitis is a desideratum at the present time. Without detracting in the least from Professor Senn's admirable groupings under the headings of anatomical, etiological, pathological, bacteriological and clinical, it must be confessed that in all probability the last-named, with perhaps some modifications, will be found most acceptable to the every-day practitioner.

Custom has sanctioned, to a certain extent, the use of the term "general septic peritonitis." The term "diffuse peritonitis," however, is more generally and logically applicable than that of "acute general peritonitis," for the reason so cogently stated by Dr. Abbe, that it is impossible in any given case to state that absolutely every portion of the peritoneum has been invaded. For this reason, therefore, the term "diffuse septic peritonitis," it would seem, is to be preferred to that of "general peritonitis."

So too, with the term "perforative peritonitis." This carries with it the etiological factor involved in its occurrence, and conveys at once the idea of the possibility of successful remedial measures and the necessity for their immediate application, if the patient is to obtain the best results from surgical intervention.

"Circumscribed," or localized, peritonitis is likewise a term which appeals to the surgical clinician. Every practitioner realizes what is to be confidently expected under conditions of strict localization of peritoneal inflammation, provided proper and timely surgical measures are introduced into the case. If a relatively positive diagnosis of localization of the peritoneal inflammation, as distinguished from the diffuse form, can be made, a weight of anxiety and responsibility is lifted from the shoulders of the attendant.

The more recently introduced term, "hæmatogenous peritonitis," likewise has its uses, although the rarity of the condition is now generally recognized. It is certainly to be preferred to the sometime popular, although awkwardly expressed, "cryptogenic septopyæmia," a term which savors, to a great extent, of an attempt to take refuge behind the barrier of a high-sounding name in order to escape the necessity of exposing our ignorance.

The frequent occurrence of septic peritonitis of puerperal origin is a sufficient warrant for the use of the term "puerperal peritonitis," aside from the fact that the condition presents striking clinical peculiarities, as well as definite therapeutical indications. The obstetric surgeon particularly will, without doubt, endorse the retention of this term in the nomenclature of disease.

Although no sharp line can be drawn between the peritoneum of the pelvis and that of the cavity of the abdomen, yet the clinical picture suggested by the term "pelvic peritonitis," if it be understood that by this is meant a peritonitis originating from the female genitals, appeals at once to the experienced practitioner. While pelvic peritonitis is circumscribed peritonitis in a sense, yet the conditions present, as well as the etiological factors introduced, differ so widely from localized peritonitis as generally understood that there would appear to be no good reason for dropping this term from general use.

The form of local peritonitis embraced under the general head of "subphrenic abscess" has only recently been removed from the class of cases which permitted of diagnosis in the dead house almost exclusively. The condition now claims attention at the hands of the clinical investigator, and instances are multiplying daily which serve to demonstrate that a proper appreciation of the conditions present is not only possible at the hands of skilled consultants, but that its recognition by the average medical attendant is demanded as well. Inasmuch as these abscesses have for their manifestation either alone, or in connection with an infection of the connective tissue proliferation involved in the formation of peritoneal adhesions, the substitution of the term "subdiaphragmatic peritonitis" for "subphrenic abscess" appeals at once to our reason and commendation.

Prognosis of the Bacterial Invasion of the Peritoneum. Inasmuch as the general concensus of opinion at the present day among investigators holds the practitioner to the view that peritonitis is exclusively of bacterial origin, the question of prognosis, in

the general sense, of infectious peritonitis, as in inflammatory infectious conditions elsewhere, simply relates to the balance to be struck between virulency and extent of infection on the one hand, and the degree of vital resistance on the other. With a small amount of even a comparatively innocuous germ present, a fatal peritonitis may follow prolonged handling and consequent extensive abrasions of the peritoneal surfaces, and a comparatively slight traumatism, in the presence of a streptococcus pyogenes infection may be followed likewise by a fatal result. Further, it has been shown by Grawitz that the peritoneum is tolerant of a certain amount of even highly infectious material, providing there is nothing present that can furnish the pabulum necessary for its growth and increase. Up to a certain point the serous membrane is capable of destroying the bacteria, but beyond this its power ceases, and the irritating properties of the toxic products of the micro-organisms assert themselves. Finally, it should be borne in mind that it is not necessary for bacteria to multiply in order to produce peritonitis. Their contact with the peritoneum under circumstances which likewise become the occasion for transudation of serum, effusion of blood, or injury to and perhaps sloughing of tissues, or the simultaneous entrance of other substances which may serve as proper nutritive material, such as fæces, affords opportunity for the production of those toxic substances upon which their irritating properties depend, without the necessity for increase in numbers of the bacteria themselves.

The methods of invasion of the peritoneum will govern largely the outcome of the infection. These methods of invasion are self-evident. They include introduction from without through wounds involving both skin and peritoneum; passage through perforation, the result of a traumatism or destructive inflammatory lesion of some hollow viscera; by penetration of the walls of the viscera because of the impairment of the nutrition of such wall; by progressive and continuous growth of bacteria in the substance of the wall of a viscus, the seat of a septic inflammation, such as the uterus; and finally by infection through the blood or lymph vessels from some more or less distant focus.

The occurrence of peritonitis without the actual presence of bacteria is of great interest in this connection. This may occur if their toxins reach the serosa, which they may do, by penetration of the visceral walls without the presence of any actual lesion. It is now likewise believed that the bacteria themselves may pass through a visceral wall without multiplication as well as without exciting any

apparent disturbances in those tissues, as in the instance of the wall of a hernial sac.

A further question of great interest in connection with this subject is that of the germicidal power of the serous effusion of the peritoneal cavity. Like the blood serum elsewhere, the serum of the peritoneum possesses to a certain extent the power of destroying even the most virulent micro-organisms. There is a limit to this power, however, and when this is reached the bacteria remaining undestroyed find at once the proper pabulum for their numerical increase, as well as the development of the toxic substances upon which their pathologic properties depend. To this germicidal power of the peritoneal effusion, upon the one hand, and the now well-known fact, first established by the experiments of Wieland, that the bacteria in encapsulated abscesses in the peritoneal cavity tend to die out, upon the other, is to be attributed the occasional recoveries ensuing in instances where the operative procedure reveals a large amount of thin and opaque serum, the result of a rupture of a seropurulent intraperitoneal collection, with an appendical lesion as the original focus of infection. The intestines float in an abundance of this fluid, yet both the visceral and the parietal peritoneum are scarcely injected, much less actively inflamed. A number of such instances have come under my observation, in which uninterrupted recovery has followed incision, removal of the original focus of infection, and gauze drainage. In none of these cases have I been able to directly demonstrate bacteriologically the sterility of the abdominal fluid, but this does not alter the fact that the recoveries were due either to the germ-resisting and destroying powers of the peritoneum, to a slow process of sterilization of the contents of the original encapsulation, or both. Besides, no amount of negative evidence in a test tube appeals so strongly to the surgeon's senses as the presence of normal intestines floating about in sero-pus, the latter bathing everything in sight, and yet not the slightest trace of infection, as evidenced by tinge of abnormal hue to be seen, to say nothing of the circumstance of recovery without the supervention of the first symptom of local or constitutional disturbance.

The most dangerous of these modes of entrance is that which involves a perforation of the intestinal wall of the small intestine, and the least dangerous that which occurs in connection with a wound of the abdominal wall. In the first-mentioned not only is there a great number of bacteria which escape into the peritoneal cavity, but these are most virulent in character and are accompanied

by toxins, the result of their growth in the intestinal canal. There likewise is deposited upon the peritoneal surfaces fecal matter, which acts in the dual capacity of a pabulum for the growth of the bacteria and an irritant which excites serous exudation. The latter, as soon as its germicidal power is exhausted, also becomes a rich culture medium for the propagation of the germs. It is this "concatenation of adverse circumstances" which accounts for the high mortality following this accident. The size of the perforation and the rapidity with which the contents of the intestine escape will govern, to some extent, the prognosis in cases of intestinal perforation. When the small intestine is the seat of the perforation, the fecal matter may be poured out rapidly and a diffuse septic peritonitis from mixed infection promptly follow. In perforation involving the large intestine the exit of fecal matter may be comparatively slow; adhesive protective barriers are thrown out before diffusion of the infecting agents occurs. The infection is thereby limited and a localized suppurative peritonitis follows, as for instance in peri- and para-cæcal abscess (suppurative perityphilitis).

If, however, a diffuse instead of a circumscribed suppurative inflammation follows the infection, as occurs in the great majority of perforations involving the small intestine, there occurs a train of most dangerous symptoms, due to the absorption of septic material from the extensive surface area of this enormous lymph-sac.

The least dangerous of the modes of entrance is that which occurs in connection with a wound of the abdominal wall. But a comparatively small number of bacteria are introduced in this manner, probably not more, in the majority of instances, than the peritoneum itself is able to destroy by its serum. These circumstances explain the comparative immunity from danger of many cases of abdominal section for non-suppurative lesions of the uterine appendages at the hands of surgeons who boast of their neglect to protect their patients by the employment of an anti-bacterial operative technique.

Concomitant circumstances may arise to render the last mentioned mode of bacterial invasion most dangerous, as for instance the simultaneous occurrence of contusion of the peritoneal surfaces, laceration of some of the hollow viscera, the occurrence of hemorrhage or the presence of a foreign body. Per contra, it may happen, as before stated, that a small perforation with slow escape of the contents of the intestine may lead to encapsulation by adhesive barriers and protection of the general peritoneal cavity.

Between these two extremes are to be mentioned, in the order of their gravity, first, invasion through perforations or wounds of viscera other than intestine, including the kidneys, pancreas, and the biliary ducts, ureters, etc., and the eruption of a neighboring abscess, save only when the pus of the latter is sterile. Second, the entrance of bacteria, by continuous inflammatory growth, through the walls of a portion of the intestinal canal or other hollow viscera. While the mode of invasion here is dangerous, from the fact that a large number of bacteria may find their way to the peritoneal surface in a short time, the method of entrance may be resisted by the formation of adhesions upon the menaced serous surface. As an instance of this manner of bacterial invasion may be mentioned the successive occurrence of endoappendicitis, parietal appendicitis, and finally periappendicitis. Third, infection of the peritoneum by way of the Fallopian tubes. The comparatively lessened dangers of this route of infection relate (a) to the fact that the source of bacterial supply is not large, the endometrium possessing a high degree of vital resistance and its secretion rendering its cavity in most instances sterile, as shown by Warbasse's investigations; (b) to the relatively low grade of virulency of the two kinds of bacteria most frequently found in tubal infection, namely, the gonococcus and the bacillus tuberculosis; and (c) ample opportunity is usually afforded for the production of competent adhesive barriers, including those which seal the opening of the tube and confine the infection to the latter and its immediate vicinity. Fourth, those cases in which the bacterial migration takes place through the wall of the intestine as the result of nutritive disturbances of the latter, such, for instance, as occurs in strangulated hernia. Comparatively few bacteria escape in this manner, while at the same time there is a copious effusion of serum. The germicidal power of the latter is sufficient to destroy the bacteria if the latter are not too numerous. This accounts for the fact that in later years, other sources of infection being guarded against, relatively few cases of diffuse peritonitis follow operations for strangulated hernia, unless gangrene and perforation of the bowel wall has taken place.

In estimating the prognosis of peritonitis, the practical surgeon will be compelled to take into account the source and virulency of the infection, the mode of entrance of the bacteria, the concomitant circumstances of injury to the viscera, hemorrhage and large serous exudations, and last, but not least, the extent of the localization of the infection, on the one hand, and its generalization, on the

other. A case of the most violently infectious peritonitis, if localized, may recover, provided proper and timely surgical aid be rendered and its suppurative products evacuated. It is equally true, likewise, that a comparatively mild, yet widely diffused, infection may destroy life, the general system becoming finally overpowered by the toxic products furnished by absorption from involved extensive area of serous membrane.

Treatment. With the measures designed to meet the conditions present in a localized suppurative peritonitis, I need scarcely detain you in this discussion. Free incision and proper drainage cover the ground completely. The large majority of cases so treated recover as promptly and satisfactorily as where the same principles of treatment are applied to a suppurative collection elsewhere. In the very recent past, the almost unqualifiedly favorable prognosis which the surgeon was able to give, in cases of localized suppurative peritonitis, was as absolutely reversed in the case of advanced diffuse septic peritonitis, as is the day removed from the night, no matter what treatment was pursued. So great are the difficulties in the way of the complete emptying, disinfecting and draining of the peritoneal cavity, and so dire are the effects upon the vital centers of the enormous quantities of toxic products which find their way from the extensive area involved in the infection, that the surgeon has been almost absolutely without resource in the face of this condition of affairs. He is handicapped at every turn. Persistent vomiting and the early intolerance of the rectum to nutrient enemata prevent him from reinforcing the patient's fast-waning strength, and paralysis of peristalsis robs him of the most efficient non-operative method of drainage of the peritoneum. The passage of fecal matter into the stomach adds the damaging effects of stercoremia to the already existing toxemia. These, together with the weak and rapid pulse, vaso-motor paralysis, and mental hebitude, combine to stamp the condition as almost absolutely hopeless.

Before these symptoms of systemic infection have advanced to this stage, however, there is a period varying from a few hours to a day or two, during which these symptoms are less aggravated or perhaps absent, and yet sufficient evidence of peritoneal inflammation is present to base a diagnosis upon. Herein resides the surgeon's opportunity. In proportion to the ability on the part of the medical attendant to recognize the true state of affairs early, and his willingness to share the responsibility of the case with the surgeon, on the one hand, and the skill, judgment, and particularly moral

courage of the latter, on the other, will the prognosis in diffuse peritonitis improve.

During the past two years there have been a number of cases of diffuse septic peritonitis operated upon successfully, and the matter has reached a stage where the surgeon's margin in escaping responsibility in not operating is becoming narrower and narrower. While there may be cases here and there where the patient's doom is sealed from the very commencement, yet, in view of the knowledge derived from the bacteriological laboratory and experimentation upon animals, it is difficult to conceive of such a case. If the Lembert suture could close the perforation immediately upon its being made, or the gauze drain carry off the septic products as soon as these were produced, other things being equal, what would kill the patient?

Still another ray of light has been cast into this dark recess of the surgeon's domain. Encouraged by the success that has followed the antitoxin serum treatment of diphtheria, experimenters have sought to produce an antitoxin to other pathogenic bacteria. The fact that the streptococci are of such importance as etiological factors in phlegmonous inflammation, and are found so frequently associated with other micro-organisms in the most severe and complicated forms of infectious disease, have led to a careful study of this microbic infecting agent. As a result of these studies, much has been learned from the biological standpoint; what is of greater importance, however, if the hope of the present is realized in the future, an antitoxin has been developed to this germ.

Although not all of the experiences with the treatment of septic peritonitis by means of the streptococcus antitoxin have been favorable, so far as a successful result is concerned, yet these have been such as to warrant investigation of this as a means of combatting the general infection.

It would be out of place in a discussion of this kind to enter elaborately into the subject of orrhotherapy, but I may be pardoned if my estimate of the importance of the subject leads me to refer to some recent experiences of some of my colleagues in New York, as well as of my own. The interest in these cases is enhanced by the fact that some of them have not yet been published.

Dr. Howard Lilienthal has kindly placed at my disposal abstracts of three cases bearing upon this question. The first was a case of perforative appendicitis followed by diffuse septic peritonitis. At the operation (June 1896) pus and feces were present in the peritoneal cavity. One injection of 12.5 c.c. Gibier's streptococcus

antitoxin was administered. A secondary intraperitoneal abscess required intervention some days later. The recovery was complete. The second was a case of diffuse peritonitis from disease of the uterine appendages treated by operation. Temperature dropped to normal after one injection of streptococcus antitoxin (Park, Davis & Co.'s). Death from paralysis of peristalsis. The third case was that of a boy of 10, who was suffering from diffuse peritonitis from appendicitis and was almost moribund at the time of the operation. The antitoxin used was that of Park, Davis & Co. The patient died.

In the case of Dr. Lilienthal's first patient who recovered, it will be noted that a secondary intraperitoneal abscess required interference some days later. This suggests that the original infection, although probably wide, was not general, in the sense of a diffuse and unlimited septic peritonitis.

The case reported by Dr. Egbert H. Grandin* is worthy of comment. The case was one of suppurative peritonitis due to a gangrenous and perforated appendix, which was removed by operation. The pulse was 90 and the temperature 100 Fahr. Hot salt water irrigation and gauze drainage from the median wound were practiced. After a few days a pus cavity containing over a pint was evacuated on the left side, just above Poupart's ligament, a counter-opening being made at the same time into the vagina, thus establishing through drainage. Upon the following day another series of pus pockets was opened, irrigated and drained. Upon the next succeeding day another incision, uniting the two last, was made upon the left side of the abdomen. It was upon this day that the streptococcus antitoxin was first used.

This patient recovered. In view of the fact that the reporter, in the early part of this article, expresses a doubt as to whether the entire abdomen had been infected, and later on relates how he opened and drained circumscribed collections of sero-pus,—and the further fact that these most valuable and ordinarily efficient measures in circumscribed peritonitis had been instituted before the administration of the serum, there must remain a very decided doubt as to the part which the antitoxin played in bringing about the favorable result.

Dr. M. R. Richard, of New York, in a personal communication, gives me the details of a most interesting experience with the serum of Dr. Marmorek, of the Pasteur Institute

* Medical Record, New York, 1897.

in Paris. The patient was also seen by Drs. Mundé and Brettauer. The case was one of post-puerperal infection. Thorough curettment under chloroform failed to effect any amelioration in the symptoms. Five days afterward the temperature was 106.2° Fahr., the pulse 150, and the respirations 46. There was a fall of 2° one hour after the first 10 c.c. injection of the Marmorek serum, and a still further fall of 2.2° after the second, making a total fall of 3.8° in 12 hours. A fall of 6° took place in 31 hours. This patient recovered.

Recovery in puerperal peritonitis takes place with just sufficient frequency to cast a doubt upon the influence of the serum in this case, although the prompt subsidence of the alarming symptoms following the injections would be difficult of explanation upon any other hypothesis.

Dr. Van Arsdale reported two cases of what he terms "general purulent peritonitis," at the April meeting of the Surgical Section of the New York Academy of Medicine. In the first, a 15-year-old girl, a sero-purulent collection of appendicular origin had invaded the peritoneum. The temperature was 103.6° Fahr., pulse 140 and respirations 32. Counter-incisions were made and irrigation with hot salt solution practiced. During the irrigation the patient was held in the upright position. Drainage tubes were inserted in both sides. The first injection of antitoxin (6 c.c.) was made 14 hours after the operation. 6 hours later a second injection (8 c.c.) was used. A third injection was made the next day of 7 c.c. The bowels were moved by ox gall enema 24 hours after the operation, and later on by the administration of calomel and citrate of magnesia. The temperature gradually came down to the normal, the general condition and pulse improved, and an uninterrupted recovery ensued. She was discharged from the hospital February 20, just one month after the attack.

The second case was a 37-year-old woman who was attacked on January 13, 1897, with a gangrenous cholecystitis. The temperature was 99°, pulse 140 and respiration 32. The operation revealed, as expressed by Dr. Van Arsdale, "a general sero-purulent peritonitis." The gall bladder was opened and drained. Four hours after the operation the temperature rose to 103.4°, the pulse, almost imperceptible, to 180 and the respirations to 50. At this time 3½ pints of a .6% salt solution were infused in the right median basillic vein. Twelve hours after the operation the first injection of 9 c.c. of streptococcus antitoxin was used, after which another intravenous infusion of 3 pints of salt solution was given. During the following

20 hours the temperature remained between 102° and 103°. During this time two more injections of 8 c.c. each of the serum were given. Upon the fifth day the temperature was down to 101°. From this time the improvement was gradual. She was out of bed on February 13, just one month from the commencement of the attack.

Dr. Van Arsdale remarks that no special reaction was observed after each injection, that might have been attributed to the antitoxin.

While these cases are exceedingly interesting and suggestive, neither of them come within that most desperate class of cases in which there is a direct infection from the interior of the intestinal canal into the cavity of the peritoneum, and an indubitable diffuse, unlimited septic peritonitis present. It has been my great misfortune to meet with a number of the latter cases, and their almost unexceptionally fatal termination led me, in the last which fell under my care, to endeavor to overcome the systemic infection by the employment of the streptococcus antitoxin, relying upon widely distributed glass tube and wicking drainage combined to combat the local septic conditions.

My own case is as follows:

A. V., aged 29, was seen by me in consultation late in the evening of April 10th, 1897. A history of at least three previous attacks of appendicitis, occurring within the last four years, was obtained; 28 hours prior to my visit the first symptoms of the present attack of appendicitis began. These progressed rapidly, and perforation had evidently taken place within 12 hours of the commencement of the attack. Efforts to obtain catharsis by means of calomel and sulphate of magnesia had proved ineffectual. When seen by me the temperature was 103.5° Fahr. and the pulse 130. The abdomen was distended, everywhere tympanitic, and extremely rigid. Maximum point of tenderness just below the umbilicus.

He was removed to the Brooklyn Hospital and the abdomen opened in the median line. A diffuse septic peritonitis, with pus and fecal matter in the cavity of the peritoneum, was found. About 15 inches of ileum, bound firmly by adhesions in a mass in the median line, was bluish black in color, and necrotic in spots. Parting the adhesions, a gangrenous and perforated appendix was discovered and removed. The cavity of the abdomen was thoroughly irrigated with sterilized salt solution, the incision being extended to gain access to the regions of the spleen and liver. The cavity was drained by gauze in four directions, supplemental incisions being made for the purpose, i. e., in the hepatic, splenic and iliac fossæ; gauze drains were also led out of the upper and lower

angles of the median wound. Copious absorbent dressings were applied.

Within 6 hours of the operation the temperature dropped to 98.6°, the pulse to 110. At the end of 12 hours the temperature was found to be rising, having reached 100° and the pulse 140. At this time 12.5 c.c. of Gibier's streptococcus antitoxin was injected in the left buttock. In spite of this, however, the temperature rose in 8 hours to 101.2°. A second injection of 12.5 c.c. was now given. In the course of the following 8 hours the temperature had fallen a trifle over 1 degree, and the pulse to 116. A third injection was followed by another fall of .6°, the pulse rate being 94. In the course of the next 8 hours the temperature rose a degree, and the pulse to 116. A fourth injection of 8.3 c.c. was now administered. No change in pulse and temperature followed this injection. A fifth injection of 8.3 c.c. was given after 6 hours; this was followed by a fall of the temperature to normal, but the pulse rose to 120. An injection of 8.3 c.c. every 6 hours was followed by a temperature at practically the normal, the pulse ranging from 114 to 120, for the next 12 hours. The temperature then rose to 101°, and the pulse to 126. From this time until his death, which took place on the fifth day following the operation and the sixth of the disease, the temperature was practically uninfluenced by the serum, although the pulse rate remained in the neighborhood of 100; just before death, counted at the heart, it was 80.

Fecal vomiting, due to paralysis of peristalsis, was present at intervals for 48 hours before death. This was met with frequent lavage, the stomach tube being utilized after each lavage for the introduction of liquid food. The usual heart stimulants were likewise employed throughout the case. The *morale* of the patient was excellent until a few hours before death. There was likewise a complete absence of vaso-motor paralysis until an hour before the lethal exit. The daily excretion of urine was uninfluenced, and the slight albuminuria present before the operation was neither increased nor diminished by the treatment. 250 c.c. of the serum, in all, were used.

The autopsy revealed a gangrenous condition of the parietal and visceral layers of the peritoneum throughout almost the entire region of the small intestine. The peritoneal cavity everywhere was dry and clean. The most indubitable evidences of a diffuse, unlimited peritonitis were present.

The fact that the drainage was so complete, as revealed by the autopsy, taken in conjunction with the somewhat contradictory

results of some of the injections as compared with others, leads me to express some doubt as to the influence which the serum exercised upon the course of the case.

In perforative peritonitis, as before stated, a mixed infection is present in the vast majority of cases; while it is probably true that the streptococcus pyogenes is among the most virulent; if indeed it is not the most virulent microbic organism present under these circumstances, it is not by any means the only one capable of destroying life. With this fact before us, and the knowledge that the antitoxin of one class is powerless against another, it at once becomes evident that, in order to proceed rationally, the surgeon and bacteriologist must work side by side, an antitoxin to each pathologic bacterium being furnished, according to the findings.

And this is as it should be. The bacteriologist has been for years working out biological problems in his laboratory, but only here and there has the every-day practitioner been able to avail himself of the knowledge thus gained. Among the notable instances of the practical application of this knowledge is the treatment of diphtheria by means of the antitoxin of its own infecting agent. If the claims made for this method of treatment are well-founded, there is no reason why immunization against the toxic substances produced in the life history of other germs should not be secured, providing the law that each microbic organism is capable of producing an agent antagonistic to its own toxic products,—in other words, an antitoxin,—holds good in all cases of bacterial infection. Now let bacteriological science step forth and take its place among the specialties in practical medicine, for such a place surely awaits it. Backed by a diagnosis based upon a properly conducted bacteriological examination, reinforced by means of combating systemic infection if this occurs, and stimulated by a reasonable hope of eventually saving the patient's life, the surgeon will be emboldened to enter upon those extensive operations which, up to this time, while perfectly understood and appreciated by the bulk of the profession, have not only served to cast undeserved opprobrium upon the individual operator at the hands of the laity, but to bring into disrepute surgical science and art as well.

Dr. W. H. Welch: I should allude to one point pertinent to the discussion, although not of very great practical importance, the question as to the existence of chemical peritonitis. I quite agree with Dr. Senn and others who have spoken, that for all practical purposes we had better consider all cases as of bacterial origin.

There are certain points as regards the distribution of peritonitis that are of importance. Take those that occur after ulcer of the intestine. You may have a general circumscribed peritonitis, corresponding to the site of the ulcer, and in that exudate no microorganism whatever. As to the fact of such occurrences I have no doubt, but I must say that in order to exclude the presence of bacteria in the exudate a very careful examination must be made. Cultures are not decisive. Cultures and cover-slip preparations should be made always, but to be positive always make inoculations of animals. I have examined such cases, and there is no question of the exudate over areas of inflammation like this. Again, you may find pockets of pus with an exudate around them, a diffuse fibrinous exudate spreading over a considerable area. You may find occasionally bacteria present in the pocket of pus, but none over a considerable area of exudate surrounding that circumscribed collection of pus. You have no guarantee, therefore, of the distribution of the organism by the distribution of the exudate. This has an important bearing on the case, for the surgeon.

Dr. Abbe: Since the subject of the use of antistreptococcus serum has come up, I should like to add a few words. Nothing has been published yet that gives any hope of its value. In my own experience, of three cases since last July in which I have used it, in general peritonitis the course of the disease seemed to progress a little more rapidly perhaps than in other cases. I shall use it again, but not with the hope I had in the first few cases.

Dr. J. Taber Johnson: I would like to ask Dr. McCosh if he would kindly give us a little more in detail his method of injecting the Epsom salt solution into the intestines, whether it is done through the abdominal wall, or into the intestines direct at the time of the operation. It is a matter of great importance, as the Doctor has said, to secure early movements of the bowels. Improvement of the technique is what we all desire, and I should like to know a little more about this method, which has so much of promise in it. I have frequently given large doses of Epsom salts just before an abdominal section, and when it was retained the result was excellent.

Dr. McCosh: In reply to Dr. Johnson's inquiry, I would say that the injections were made at the time of operation, after the intestines had been removed from the abdominal cavity. The needle of a large hypodermic syringe (antitoxin syringe) is thrust into the jejunum, the opening being afterwards closed by a Lembert suture.

ADAPTATION IN PATHOLOGICAL PROCESSES.

BY WILLIAM H. WELCH, M.D.

Professor of Pathology, Johns Hopkins University.

Grateful as I am for the personal good-will manifested by my selection as President of this Congress, I interpret this great and unexpected honor as an expression of your desire to give conspicuous recognition to those branches of medical science not directly concerned with professional practice, and as such I acknowledge it with sincere thanks.

All departments represented in this Congress are working together toward the solution of those great problems—the causes and the nature, the prevention and the cure, of disease—which have always been and must continue to be the ultimate objects of investigation in medicine. It is this unity of purpose which gives to the history of medicine, from its oldest records to the present time, a continuity of interest and of development not possessed in equal degree by any other department of knowledge. It is this same unity of purpose which joins together into a single, effective organism the component parts of this Congress, representing, as they do, that principle of specialization and subdivision of labor which, notwithstanding its perils, has been the great factor in medical progress in modern times.

Medical science is advanced not only by those who labor at the bedside, but also by those who in the laboratory devote themselves to the study of the structure and functions of the body in health and disease. It is one of the most gratifying results of the rapid advance in medical education in this country during the last few years, that successful workers in the laboratory may now expect some of those substantial rewards which formerly were to be looked for almost exclusively in the fields of practical medicine and surgery. We already have abundant assurance that the steady improvement in opportunities and recompense, and other material conditions essential for the prosecution of scientific work in medicine, will enable this country to contribute to the progress of the medical sciences a share commensurate with its great resources and development in civilization.

The subject of "Adaptation in Pathological Processes," which I have selected for my address on this occasion, is one which possesses the broadest biological, as well as medical, interests. It is this breadth of scientific and practical interest that must justify my choice of a theme which involves many technical considerations and many problems among the most obscure and unsettled in the whole range of biology and of medicine.

I shall employ the epithet "adaptive" to describe morbid processes which bring about some sort of adjustment to changed conditions due to injury or disease. In view of the more technical and restricted meaning sometimes attached to the term "adaptation" in biology, objection may be made to this broad and general application of the word in pathology; but no more suitable and convenient epithet than "adaptive" has occurred to me to designate the entire group of pathological processes whose results tend to the restoration or compensation of damaged structure or function, or to the direct destruction or neutralization of injurious agents. Processes which may be described variously as compensatory, regenerative, self-regulatory, protective, healing, are thus included under adaptive pathological processes. These processes are, in general, more or less advantageous or useful to the individual; but for reasons which will be stated later the conception of pathological adaptation and that of advantage to the individual are not wholly coextensive.

Within the limits of an address I cannot hope to do more than direct attention to some of those aspects of the subject which seem to me to be of special significance. Although most striking examples of adaptation are to be sought in comparative and vegetable pathology, what I shall have to say will relate mostly to human pathology. My purpose is not to point out the beauties or the extent of adaptations in pathological processes, but rather to say something concerning the general mechanism of their production and the proper attitude of mind regarding them, and to illustrate the general principles involved by a few representative examples.

It has been contended that the conception of adaptation has no place in scientific inquiry; that we are justified in asking only by what means a natural phenomenon is brought about, and not what is its meaning or purpose; in other words, that the only question open to scientific investigation is How? and never Why? I hope to make clear by what follows in what light I regard this question, and in this connection I shall simply quote Lotze, who, beginning as a pathologist, became a great philosopher: "Every natural phenomenon may be investigated not only with reference to the

mathematical grounds of its possibility and the causes of its occurrence, but also as regards the meaning or idea which it represents in the world of phenomena."

The most wonderful and characteristic attribute of living organisms is their active adaptation to external and internal conditions in such a way as tends to the welfare of the individual or of the species. Of the countless physiological examples which might be cited to illustrate this principle, I select, almost at random, the preservation of the normal temperature of the body in warm-blooded animals under varying external temperatures and varying internal production of heat, the regulation of respiration according to the need of the tissues for oxygen, the influence of the load upon the work performed by muscles, the accommodation of the heart to the work demanded of it, the response of glands to increased functional stimulation, the adjustment of the iris to varying degrees of illumination, the influence of varying static conditions upon the internal architecture of bone.

The most striking characteristic of these countless adaptations is their apparent purposefulness. Even if it be true, as has been said by Lange, that "the formal purposefulness of the world is nothing else than its adaptation to our understanding," it is none the less true that the human mind is so constituted as to desire and seek an explanation of the adaptations which it finds everywhere in organic nature. From the days of Empedocles and of Aristotle up to the present time there have been two leading theories to explain the apparent purposefulness of organic nature—the one, the teleological, and the other, the mechanical theory. The teleological theory, in its traditional signification, implies something in the nature of an intelligence working for a predetermined end. So far as the existing order of nature is concerned, the mechanical theory is the only one open to scientific investigation, and it forms the working hypothesis of most biologists. This theory, in its modern form, seeks an explanation of the adaptations of living beings in factors concerned in organic evolution. What these factors are we know only in part. Those which are most generally recognized as operative are variation, natural selection, and heredity. That additional factors, at present little understood, are concerned seems highly probable. The acceptance of the explanation of physiological adaptations furnished by the doctrine of organic evolution helps us, I believe, in the study of pathological adaptations.

As the word "teleology" has come to have, in the minds of many, so bad a repute in the biological sciences, and as I desire, without entering into any elaborate discussion of the subtle questions here involved, to avoid misconceptions in discussing subjects whose ultimate explanation is at present beyond our ken, I shall here briefly state my opinion that all of those vital manifestations to which are applied such epithets as adaptive, regulatory, regenerative, compensatory, protective, are the necessary results of the action of forms of energy upon living matter. The final result, however useful and purposeful it may be, in no way directly influences the chain of events which leads to its production, and, therefore, the character of the result affords no explanation whatever of the mechanism by which the end, whether it appear purposeful or not, has been accomplished. In every case the ultimate aim of inquiry is a mechanical explanation of the process in question. Notwithstanding valuable contributions, especially within recent years, toward such mechanical explanations, we are still far removed from the attainment of this aim.

The knowledge of the fact that the living body is possessed of means calculated to counteract the effects of injurious agencies which threaten or actually damage its integrity must have existed as long as the knowledge of injury and disease, for the most casual observation teaches that wounds are repaired and diseases are recovered from. It is no part of my present purpose to trace the history of the numerous speculations or even of the development of our exact knowledge concerning the subjects here under consideration. I cannot refrain, however, from merely referring to the important *rôle* which the conception of disease, as in some way conservative or combative in the presence of harmful influences, has played from ancient times to the present in the history of medical doctrines. Whole systems of medicine have been founded upon this conception, clothed in varying garb. There is nothing new even in the image, so popular nowadays, representing certain morbid processes as a struggle on the part of forces within the body against the attacks of harmful agents from the outer world. Indeed, Stahl's whole conception of disease was that it represented such a struggle between the anima and noxious agents. What lends especial interest to these theories is that then, as now, they profoundly influenced medical practice and were the origin of such well-known expressions as *vis medicatrix naturæ* and *medicus est minister naturæ*.

It is needless to say that there could be no exact knowledge of the extent of operation or of the nature of processes which restore

or compensate damaged structures and functions of the body or combat injurious agents, before accurate information was gained of the organization and workings of the body in health and in disease. Although the way was opened by Harvey's discovery of the circulation of the blood, most of our precise knowledge of these subjects has been obtained during the present century, through clinical observations and pathological and biological studies. In the domain of infectious diseases wonderful and hitherto undreamed-of protective agencies have been revealed by modern bacteriological discoveries. Here, as elsewhere in medicine, the experimental method has been an indispensable instrument for discoveries of the highest importance and for the comprehension of otherwise inexplicable facts. Very interesting and suggestive results, shedding light upon many of the deeper problems concerning the nature and power of response of living organisms to changed conditions, have been obtained in those new fields of experimental research called by Roux the mechanics of development of organisms, and also in part designated physiological or experimental morphology. Although we seem to be as far removed as ever from the solution of the most fundamental problem in biology, the origin of the power of living beings to adjust themselves actively to internal and external relations, we have learned something from these investigations as to the parts played respectively by the inherited organization of cells and by changes of internal and external environment in the processes of development, growth, and regeneration.

In physiological adaptations, such as those which have been mentioned, the cells respond to changed conditions, to meet which they are especially fitted by innate properties, determined, we must believe, in large part by evolutionary factors. In considering pathological adaptations the question at once suggests itself whether the cells possess any similar peculiar fitness to meet the morbid changes concerned; whether, in other words, we may suppose that evolutionary factors have operated in any direct way to secure for the cells of the body properties especially suited to meet pathological emergencies. Can we recognize in adaptive pathological processes any manifestations of cellular properties which we may not suppose the cells to possess for physiological uses? This question appears to me to be of considerable interest. I believe that it can be shown that most pathological adaptations have their foundation in physiological processes or mechanisms. In the case of some of these adaptations, however, we have not sufficiently clear insight into the real nature of the pathological process nor into all of the physio-

logical properties of the cells concerned to enable us to give a positive answer to the question.

While we must believe that variation and natural selection combined with heredity have been important factors in the development and maintenance of adjustments to normal conditions of environment, it is difficult to see how they could have intervened in any direct way in behalf of most pathological adaptations.

An illustration will make clear the points here involved. Suppose the human race, or any species of animal, to lack the power to compensate the disturbance of the circulation caused by a damaged heart-valve, and that an individual should happen to be born with the exclusive capacity of such compensation. The chances are that there would arise no opportunity for the display of this new capacity, and it is inconceivable that the variety would be perpetuated through the operation of the law of survival of the fittest by natural selection, unless leaky or clogged heart-valves became a common character of the species. When, however, we learn that the disturbance of circulation resulting from disease of the heart-valves is compensated by the performance of increased work on the part of the heart, and that it is a general law that such prolonged extra work leads to growth of muscle, we see at once that this compensation is only an individual instance of the operation of a capacity which has abundant opportunities for exercise in normal life, where the influence of natural selection and other factors of evolution can exert their full power.

In a similar light we can regard other compensatory and functional pathological hypertrophies—indeed, I believe, also to a considerable extent the pathological regenerations, inflammation, and immunity, although here the underlying factors are, of course, different.

We may, however, reasonably suppose that natural selection may be operative in securing protective adjustments, such as racial immunity, against morbific influences to which living beings are frequently exposed for long periods of time and through many generations.

These considerations help us to explain the marked imperfections of most pathological adaptations as contrasted with the perfection of physiological adjustments, although I would not be understood to imply that the absence of the direct intervention of natural selection in the former is the sole explanation of this difference. The cells are endowed with innate properties especially fitted to secure physiological adaptations. No other weapons than these

same cells does the body possess to meet assaults from without, to compensate lesions, to restore damaged and lost parts. But these weapons were not forged to meet the special emergencies of pathological conditions. Evolutionary factors have not in general intervened with any direct reference to their adaptation to these emergencies. Such fitness as these weapons possess for these purposes comes primarily from properties pertaining to their physiological uses. They may be admirably fitted to meet certain pathological conditions, but often they are inadequate. Especially do we miss in pathological adjustments that co-ordinated fitness so characteristic of physiological adaptations. So true is this that the propriety of using such terms as compensation and adaptation for any results of pathological processes has been questioned.

A heart hypertrophied in consequence of valvular lesion does not completely restore the normal condition of the circulation. Experience has shown that a kidney hypertrophied in consequence of deficiency of the other kidney is more susceptible to disease than the normal organ. What an incomplete repair of defects is the formation of scar-tissue, and with what inconveniences and even dangers may it be attended in some situations! If we look upon inflammation as an attempt to repair injury, and, therefore, as an adaptive process, with what imperfections and excesses and disorders and failures is it often associated! How often in some complex pathological process, such as Bright's disease or cirrhosis of the liver, can we detect some adaptive features, attempts at repair or compensation, but these overshadowed by disorganizing and harmful changes!

It is often difficult to disentangle, in the complicated processes of disease, those elements which we may appropriately regard as adaptive from those which are wholly disorderly and injurious. There are usually two sides to the shield, and one observer from his point of view may see only the side of disorder, and another from a different point of view, only that of adaptation.

The conception of adaptation in a pathological process is not wholly covered by that of benefit to the individual. I understand, as has already been said, by an adaptive pathological process one which in its results brings about some sort of adjustment to changed conditions. This adjustment is usually, wholly or in part, advantageous to the individual; but it is not necessarily so, and it may be harmful. The closure of pathological defects by new growths of tissue is a process which must be regarded as adaptive. But one would hardly describe as advantageous the scar in the brain which

causes epilepsy. A new growth of bone to fill in defects is often highly beneficial; but what grave consequences may result from thickening of the skull to help fill the space left by partial arrest in development of the brain in embryonic life or infancy! We see here, as everywhere, that "Nature is neither kind nor cruel, but simply obedient to law, and, therefore, consistent."

In turning now to the more special, but necessarily fragmentary, consideration of a few of the pathological processes in which adaptation, in the sense defined, is more or less apparent, I shall have in view the answers to those two questions, What is the meaning of the process? and How is it caused? which confront us in our investigation of all natural phenomena. At the outset it must be admitted that our insight into the nature of many of these processes is very imperfect, and that here answers to the world-old riddles Why? and How? are correspondingly incomplete and liable to err.

Although almost all of the elementary morbid processes, even the degenerations and death of cells, may, under certain conditions of the body, serve a useful purpose—the pre-eminent examples of pathological adaptation, in the sense of restoration or compensation of damaged structure or function, or the direct destruction or neutralization of injurious agents, are to be found among the compensatory hypertrophies, the regenerations, and the protective processes. To this last ill-defined group I refer parasiticidal and antitoxic phenomena, and some of the manifestations of inflammation, and perhaps also of fever. In the last analysis these protective processes, no less than the others mentioned, must depend upon the activities of cells.

As it is manifestly impossible, within the limits of a general address, to attempt a detailed consideration of any large number of these adaptive pathological processes, and as such consideration would necessarily involve the discussion of many technical and doubtful points, I have thought that my purpose would be best served by the selection of a few representative examples.

The compensatory hypertrophies afford admirable illustrations of certain fundamental principles regarding adaptations in pathology which I have already stated. The hypertrophy secures a functional adjustment, often of a highly beneficial character, to certain morbid conditions. This useful purpose is attained by a succession of events determined from beginning to end by the necessary response of cells and tissues, in consequence of their inherent organization, to the changed conditions. Given the changed conditions, on the one hand, and the organization of the cells, on the other, the result

must follow as surely as night follows day, and this final result influences the preceding series of events no more in the one case than in the other. That the cells possess the particular organization determining the manner of their response to these changed conditions, and, therefore, the beneficial character of the result, is dependent upon innate properties whose fitness for the purpose doubtless has been largely fixed by evolutionary factors, operating, however, mainly in behalf of physiological functions and not directly toward pathological adjustments. In correspondence with this view we find that our knowledge of the manner of production of the compensatory hypertrophies of various organs and tissues stands in direct relation to our knowledge of the physiology of the same organs and tissues.

Those compensatory hypertrophies into the mechanism of whose production we have the clearest insight are referable to increased functional activity, and are, therefore, spoken of as work-hypertrophies. This has been proved for the muscular hypertrophies and compensatory hypertrophy of the kidney; but the demonstration is not equally conclusive for the compensatory hypertrophy of other glands. I know, however, of no instance in which this factor in the explanation can be positively excluded.

The relationship between increased functional activity and hypertrophy is so evident in many cases that there is strong presumption in favor of this explanation of those glandular compensatory hypertrophies which have not as yet been clearly referred to the class of functional hypertrophies. The very occurrence of compensatory hypertrophy of an organ may direct attention to the fact that it is endowed with definite functions, and the conditions under which the hypertrophy occurs may shed light upon the nature of these functions. I need only remind you of the significance, from this point of view, of the compensatory hypertrophy of the thyroid, adrenal, pituitary, and other glands with internal secretions. I fail to see why Nothnagel should consider *a priori* improbable the occurrence of compensatory hypertrophy of one sexual gland after loss of the other, even before sexual maturity, or why Ribbert, who has apparently demonstrated experimentally such an occurrence, should find it necessary to seek the explanation in reflex nervous influences or mere hyperæmia. The so-called secondary sexual characters and the changes following castration, including the influence upon a hypertrophied prostate, point to important, even if little understood, functions which for the present we can perhaps best attribute to so-called internal secretions of these sexual organs.

The name compensatory hypertrophy is sometimes applied to growths of tissue that merely take the place of another kind of tissue which has fallen out, as, for example, the growth of adipose tissue around a shrunken kidney or pancreas, or between atrophied muscle-fibres. Here there is only compensation of space, but no compensation of structure or function. Such hypertrophies and growths are described better as complementary than compensatory.

Familiar examples of pathological hypertrophies from increased work are the hypertrophy of the heart from valvular disease and other causes, that of the muscular coats of canals and bladders behind some obstruction, and that of one kidney after loss or atrophy of the other.

In order to understand fully the manner of production of work-hypertrophy of a part resulting from some morbid condition, it is essential to know the nature of the disturbances induced by the underlying morbid condition, how these disturbances excite increased functional activity of the part which becomes hypertrophied, and what the relation is between this greater activity and the increased growth of the part.

It is impossible on this occasion to go through the whole list of compensatory hypertrophies with reference to the application of these principles. In no instance can the requirements stated be completely met in the present state of our knowledge. It will suffice for an understanding of the principles involved, and it is only with these that I am now concerned, if I take a concrete example. I select the classical and best studied one—compensatory hypertrophy of the heart. I trust that I shall be pardoned for selecting so commonplace an illustration, as the main points involved must be familiar to most of my audience; but it is possible that the application made of them may not be equally familiar. The only matters essential to my present line of argument are the mechanism of production of the hypertrophy and the general character of the adaptation thereby secured.

The heart, like other organs of the body, does not work ordinarily up to its full capacity, but it is capable of doing at least three or four times its usual work. The excess of energy brought into play in doing this extra work is called conveniently, although not without some impropriety, "reserve force." It has been proved experimentally that this storehouse of reserve power is sufficient to enable the healthy heart, at least that of a dog, to accommodate itself at once or after a few beats to high degrees of insufficiency or obstruction at its valvular orifices without alteration in the mean pressure

and speed of the blood in the arteries. But even so tireless and accommodating an organ as the heart cannot be driven at such high pressure without sooner or later becoming fatigued, and consequently so dilated as to fail to meet the demands upon it. If it is to continue long the extra work, it must receive new increments of energy.

The cardiac muscle is far less susceptible to fatigue than the skeletal muscles, but that it may become fatigued seems to me clear.

Leaving out of consideration some doubtful causes of cardiac hypertrophy, such as nervous influences, the various morbid conditions which lead to this affection are such as increase either the volume of blood to be expelled with each stroke, or the resistance to blood-flow caused by the pressure in the arteries or by narrowing at one of the valvular orifices, or both. Unless some regulating mechanism steps in, each of these circulatory disturbances must increase the resistance to contraction of the cardiac muscle, and it is evident that the heart must do extra work if it is to pump the blood through the arteries with normal pressure and speed. It is, however, no explanation of this extra work simply to say that it occurs because there is demand for it. Increased work by the heart in cases of disease of its nutrient arteries would often meet a most urgent demand on the part of the body, but here the heart flags and fails.

The physiologists have given us at least some insight into the mechanism by which the heart responds through increased work to the circulatory disturbances which have been mentioned. These disturbances all increase the strain on the wall of one or more of the cavities of the heart; in other words, increase the tension of the cardiac muscle, in much the same way as a weight augments the tension of a voluntary muscle. Now it is a fundamental physiological law that with a given stimulus greater tension of a muscle, within limits, excites to more powerful contraction, and thus to the performance of greater work. It seems clear that this law applies to the muscles of the heart, as well as to voluntary muscle. We do not know precisely how increased tension facilitates the expenditure of greater muscular energy.

Another well-known fact in the mechanics of muscle is of importance in this connection. With increase of muscular tension under a given stimulus a point is reached where the extent of contraction is diminished, although the mechanical work done, determined by multiplying the height to which the load is lifted by the weight of the load, is increased. This law applied to the heart,

whose contractions are always maximal for the conditions present at any given time, signifies that, with increased resistance to the contraction of the muscular wall of one of its cavities, this cavity will empty itself during systole less completely than before. In other words, dilatation occurs, and, as has been shown by Roy and Adami, to whom we owe important contributions on this as well as on many other points relating to the mechanics of the heart, dilatation regularly antedates hypertrophy. This primary dilatation, however, is not to be looked upon as evidence of beginning heart-failure, for, as these investigators have pointed out, it is within limits only an exaggeration of a physiological condition, and can be subsequently overcome by hypertrophy, which, in consequence of increase in the sectional area of the muscle, lessens the strain upon each fibre, and thereby permits it to shorten more during contraction. If this result is completely secured, we have simple hypertrophy. More often the dilatation remains, and must necessarily remain, and we have excentric hypertrophy, which secures, for a time at least, adequate, but I do not think we can say perfect, compensation.

The weight of existing evidence favors the view that the power of the heart to adapt its work to the resistance offered resides primarily in its muscle-cells, and not in intrinsic or extrinsic nervous mechanisms, although doubtless these latter in various ways, which cannot be here considered, influence and support this regulating capacity. Nor can I here pause to discuss the influence of blood-supply to the cardiac muscle upon the force of ventricular contraction, although Porter has demonstrated that this is important.

In tracing the steps from the primary morbid condition to the final hypertrophy, we have thus far had to deal mostly with known mechanical factors. We now come to the question, How does increased functional activity lead to increased growth?

Inasmuch as greater functional activity is regularly associated with a larger supply of blood to the more active part, the view is advocated by many that the increased growth is the direct result of this hyperæmia, and one often encounters, especially in biological literature, this opinion expressed as if it were an indisputable fact. There is, however, no conclusive proof of this doctrine, and many facts speak against it. The examples from human pathology commonly cited to support the doctrine that local active hyperæmia incites growth of cells are, so far as I am able to judge, complicated with other factors, such as injury, inflammation, or trophic dis-

turbances. Transplantation-experiments, such as John Hunter's grafting the cock's spur upon the cock's comb, sometimes adduced in this connection, are not decisive of this question, for here a new circumstance is introduced which some suppose to be the determining one for all morbid cell-growth, namely, the disturbance of the normal equilibrium between parts. Local active hyperæmia may exist for a long time without evidence of increased growth in the congested part. To say that the hyperæmia must be functional is at once to concede that it is not the sole factor. Experiments from Bizzozero's laboratory, by Morpurgo and by Penzo, indicate that local hyperæmia due to vaso-motor paralysis, or to the application of heat, favors cell-multiplication in parts where proliferation of cells is a normal phenomenon or is present from pathological causes, but that it is incapable of stimulating to growth cells whose proliferating power is suspended under physiological conditions, as in developed connective tissue, muscles, and the kidneys.

It has been usually assumed that the way in which local hyperæmia may stimulate cell-growth is by increasing the supply of nutriment to cells. The trend of physiological investigation, however, indicates that the cell to a large extent regulates its own metabolism. If the cell needs more food, of course it cannot get it unless the supply is at hand, and in this sense we can understand how a larger supply of blood may be essential to increased growth; but this is a very different thing from saying that the augmented blood-supply causes the growth.

It is by no means clear that the question as to the influence of increased blood-supply upon cell-growth is identical with that of increased lymph-supply. The experiments of Paschutin and of Emminghaus, from Ludwig's laboratory, nearly a quarter of a century ago, indicate that local hyperæmia due to vaso-motor paralysis does not, as a rule, increase the production of lymph; and more recent experiments, although not wholly concordant in their results upon this point, tend to the same conclusion. Functional activity, however, has a marked influence in increasing the quantity and affecting the quality of lymph in the active part. Our knowledge of the physical and chemical changes in working muscles and glands enables us to conceive why this should be so, for all are now agreed that the formation of lymph is due not simply to filtration from the blood-plasma, but also to diffusion, and some believe likewise to active secretion by the capillary endothelium. Doubtless arterial hyperæmia is essential to the maintenance of the increased flow of lymph in working organs.

There are difficulties in the way of supposing that increased supply of lymph in itself furnishes the explanation of cell-growth, and especially of that which characterizes hypertrophy of muscles and glands. Pathologists have frequent opportunities to study the effects of all degrees of increased production and circulation of lymph associated with venous hyperæmia. A kidney or a muscle may from this cause be subjected for months and years to an excess of lymph-flow, but there is no demonstration of any consequent hypertrophy or hyperplasia of renal epithelium or muscle-cell. It is true that the chemical composition of the lymph is not the same as that of lymph resulting from increased function, and it is possible that in this chemical difference lies the kernel of the whole matter. It may also be urged that in venous hyperæmia there are circumstances which restrain or prevent growth. Nevertheless, if overfeeding, merely in consequence of increased supply of nutriment, were the real explanation of work-hypertrophies, one would expect to find some evidence of this in the class of cases mentioned.

Ribbert has recently given a new shape to the doctrine that local hyperæmia excites growth. While rejecting the usual explanation that it does so by supplying more food, he contends that distention of the blood vessels and lymph-spaces, by mechanically disturbing the mutual relations of parts, removes obstacles to growth. This theory cannot be advantageously discussed until the fact is first established that uncomplicated local hyperæmia does incite growth.

As the matter now stands, it seems to me that any satisfactory explanation of the cell-growth causing work-hypertrophies must start from physical or chemical changes in the muscle- or gland-cell itself directly connected with the increased function. These changes are the *primum mobile*, and, however important increased supply of blood or lymph may be in the subsequent chain of events, it is not the determining factor. The whole problem is part of the general one of the causes of pathological cell-growth, to which I shall have occasion to refer again.

It is interesting to note that not all kinds of excess of functional activity lead to hypertrophy. A heart may beat for years faster than normal without becoming hypertrophied. Small movements of muscle, often repeated, do not cause hypertrophy. It would appear that the amount of work done in each functional act must attain a certain height in order to stimulate growth. On the other hand, if the muscle be stretched beyond certain limits, it does not hypertrophy; on the contrary, it may atrophy, as may be seen in greatly

distended canals and cavities with muscular walls. This behavior is also in accordance with physiological observations.

The compensatory hypertrophy of muscle seems to be due mainly to increase in the size of cells, although there are observations indicating that they may also multiply. That of most glands is referable to increase both in number and size of cells. Within four or five days after extirpation of a kidney karyokinetic figures may be found in increased number in the cells of the remaining kidney.

The general character of the adaptation secured by compensatory hypertrophy of the heart is sufficiently well-known. I wish to point out certain of its imperfections. I shall not dwell upon the well-known abnormal conditions, with their remote consequences, of the systemic or pulmonary circulation, which are present during the stage of compensation, nor shall I speak of the various circumstances which may interfere with the establishment of compensatory hypertrophy.

The muscle of a hypertrophied heart is sometimes compared to that of the blacksmith's arm, and the statement is made that there is no reason inherent in the muscle itself why the one should fail more than the other. This may be true, but it is not self-evident. Exercise may influence in various ways the nutrition, function, and growth of muscle as well as of other parts. Mere increase in bulk is a coarse effect. Quality may be improved as well as quantity. The biggest muscle is not necessarily the best or the most powerful. As every trainer knows, various conditions under which work is done influence the result. Increase in the reserve energy of the heart, secured by judicious exercise—and this is the main factor in endurance—probably cannot be attributed mainly to hypertrophy; indeed, enlargement of this organ from exercise is often a serious condition. Much more might be said in this line of thought, but I have indicated why it seems to me unjustifiable to assume, without further evidence, that the condition of the muscle in pathological hypertrophies is necessarily identical in all respects with that in physiological hypertrophies.

There is an important difference in the working-conditions between most hypertrophied hearts and the normal heart. Although the maximal available energy of a hypertrophied heart during compensation is greater than that of the normal heart, clinical experience shows that in the majority of cases the energy available for unusual demands—that is, the so-called reserve force—is less in the former than in the latter. Sometimes, especially when the hypertrophy has developed in early life, the hypertrophied heart is at no dis-

advantage in this respect. As pointed out with especial clearness by Martius, the significance of this alteration in the ratio normally existing between the energy expended for ordinary needs and that available for unusual demands, is that it furnishes an explanation of the greater liability of the hypertrophied heart to tire upon exertion. Fatigue of the heart is manifested by dilatation of its cavities, and when this dilatation from fatigue is added to that already existing in most cases, relative insufficiency of the mitral or tricuspid valve is likely to occur, and the compensation is, at least for a time, disturbed. The circulation through the coronary arteries, whose integrity is so important for the welfare of the heart, is impaired, and a vicious circle may be established. Notwithstanding the valuable contributions from the Leipzig clinic as to the frequency of various anatomical lesions in the muscle of hypertrophied hearts, it does not seem to me necessary to have recourse to them as an indispensable factor in the explanation of the breakage of compensation; but I shall not here enter into a discussion of the general subject of the causes of failure of compensation.

I have described with some detail, although very inadequately, the manner of production of compensatory hypertrophy of the heart, in order, by this representative example, to make clear what seem to me to be certain general characteristics of many adaptive pathological processes, and I beg here to call attention especially to the following points. As has been emphasized by Nothnagel and others, no teleological idea or form of language need enter into the explanation of the mechanism of the process. The final result is the necessary consequence of the underlying morbid conditions. We have satisfactory mechanical explanations for essential steps in the process, and there is no reason to assume that other than mechanical factors are concerned in those vital manifestations which at present we are unable to explain by known physical and chemical forces. The properties of the cells which determine the character of their response to the changed conditions are none other than their well-known physiological properties. The adaptation finally secured, admirable as it is in many respects, and perhaps adequate for long and active life, is generally attended with marked imperfections, and, strictly speaking, is not a complete compensation. It does not present that co-ordinate and special fitness which we are accustomed to find in physiological adaptations, for the explanation of which so much has been gained by the study of the factors concerned in organic evolution.

It may be argued that under the circumstances no better kind or

degree of adaptation can be conceived of than that which actually occurs, and that the operation of evolutionary factors, with especial reference to the adjustment of the organism to the conditions causing cardiac hypertrophy, could not secure any better result. I think that it is not difficult to conceive how improvements might be introduced. It is, however, permissible to suppose that the introduction into the workings of the organism of some better mechanism to compensate the morbid conditions, might be at the sacrifice of more important physiological attributes of the body. More perfect pathological adaptations might in many instances involve a deterioration of the physiological characters of the species. It is often the case that the more highly organized living beings lack some capacity possessed by those lower in the scale of organization to resist or compensate injury and disease. This is notably true of the power to regenerate lost parts. It is, however, along the lines of improvement in the physiological characters of the individual or species that the opportunity often lies for securing increased resistance to disease or better pathological adaptations.

It would be interesting to continue our consideration of the compensatory hypertrophies by an examination of those of glandular organs from points of view similar to those adopted for the heart. For the kidney, at least, the materials are at hand for such a purpose; but, as I desire, in the limited time at my disposal, to touch upon other varieties of pathological adaptation, I must refer those interested especially to the investigations of Grawitz and Israel, Ribbert, Nothnagel, and Sacerdotti as to the conditions underlying compensatory hypertrophy of the kidney. I can likewise merely call attention to the interesting researches of Ponfick upon the most wonderful of the compensatory hypertrophies in higher animals, that of the liver. Ponfick, as is well known, has demonstrated that after removal of three-fourths of this organ new liver-substance, with normal functions, is recreated from the remainder and to an amount nearly equalling that which was lost.

The chapter of pathological adaptations in bones and joints I shall leave untouched, notwithstanding the admirable illustrations which might be drawn from this domain.

There is no more fascinating field for the study of pathological adaptations with reference to the mechanical factors involved than that furnished by the blood vessels, as has been shown especially by the brilliant researches of Thoma. With wonderful precision can a vessel or system of vessels adjust itself to changes in the pressure, velocity, and quantity of blood, and thereby serve the needs

of the tissues for blood. Under pathological, as well as physiological conditions, this adjustment may be brought about not only through the agency of vaso-motor nerves and the physical properties of the vascular wall, but also, when the necessity arises, by changes in the structure of the wall.

The changes in the circulation introduced by the falling out of the placental system at birth are essentially the same as those resulting from amputation of an extremity, and the consequent alterations in the structure of the umbilical artery are identical with those in the main artery of the stump after amputation. The closure of the ductus Botalli and the ductus venosus soon after birth, and, still better, transformations of vessels in the embryo, furnish physiological paradigms for the development of a collateral circulation. Many other illustrations might be cited, did time permit, to show that in the processes of normal development, growth and regressive metamorphosis of parts, both before and after birth, and in menstruation and pregnancy, changed conditions of the circulation arise analogous to certain ones observed under pathological circumstances, and that the mode of adjustment to these changes by means of anatomical alterations in the vessels may be essentially the same in the physiological as in the morbid state. I see in these facts an explanation of the relative perfection of certain vascular adaptations to pathological or artificial states, as may be exemplified by changes in a ligated artery and by the development of a collateral circulation. The mechanisms by which the adjustments are secured have, in consequence of their physiological uses, for reasons already explained, a special fitness to meet certain pathological conditions. That this fitness should be greater in youth than in old age is in accordance with laws of life, indicated with especial clearness by Minot in his interesting studies on "Senescence and Rejuvenation."

But these mechanisms are not equally well adapted to meet all morbid changes in the vessels. Although Thoma's interpretation of the fibrous thickening of the inner lining of vessels in arterio-sclerosis and aneurism as compensatory, or, as I should prefer to say, adaptive, is not accepted by all pathologists, it seems to me the best explanation in many cases. But the adaptation, if it be such, is here usually of a very imperfect nature, and it is not surprising that it should be so, when one considers the improbability of any mechanism developing under physiological conditions which should be specially fitted to meet the particular morbid changes underlying aneurism and arterio-sclerosis.

I shall not be able to enter into a consideration of the mechani-

cal factors concerned in adaptive pathological processes in blood vessels, although perhaps in no other field are to be found more pertinent illustrations of the views here advocated concerning pathological adaptations. The whole subject has been studied from the mechanical side most fully and ably by Thoma, whose four beautifully simple histo-mechanical principles are at any rate very suggestive and helpful working-hypotheses, even if it should prove, as seems to me probable, that they are too exclusive. I shall call attention in this connection only to the inadequacy of the old and still often adopted explanation of the development of a collateral circulation. The rapidity with which a collateral circulation may be established after ligation of a large artery, even when the anastomosing branches are very small, is known to every surgeon. This was formerly attributed to increase of pressure above the ligature; but this rise of pressure has been shown to be too small to furnish a satisfactory explanation, and Nothnagel has demonstrated that there is little or no change in the calibre of arteries coming off close above the ligature unless they communicate with branches arising below the ligature. Von Recklinghausen several years ago suggested a better explanation. The bed of the capillary stream for the anastomosing arteries is widened by ligation of the main artery, inasmuch as the blood can now flow with little resistance from the capillaries of the anastomosing branches into those of the ligated artery. The result is increased rapidity of blood-flow in the anastomosing vessels. According to one of Thoma's histo-mechanical principles, increased velocity of the blood-current results in increased growth of the vessel-wall in superficies—that is, in widening of the lumen. The tension of the vessel-wall, which is dependent on the diameter of the vessel and the blood-pressure, is, according to Thoma, thus increased; and, according to another of his principles, this greater tension results in growth of the vascular wall in thickness. The changes in the walls of the anastomosing vessels seem to me best interpreted as referable to a genuine work-hypertrophy, a conception which has already been advanced by Ziegler.

The pathological regenerations constitute a large group of adaptive morbid processes of the highest interest. Their study has become almost a specialized department of biology, and occupies a very prominent place in the extensive literature of recent years relating to experimental or physiological morphology. It has revealed in unexpected ways the influence of external environment upon the activities of cells, as is illustrated in a very striking manner by Loeb's studies of heteromorphosis.

Although the capacity to regenerate lost parts must reside in the inherited organization of the participating cells, there are observations which seem to indicate that in the lower animals this capacity may exist independently of any opportunity for its exercise during any period of the normal life of the individual or species or their ancestors, including the period of embryonic development. This is the inference which has been drawn from Wolff's observation, that after complete extirpation of the ocular lens with the capsular epithelium in the larval salamander, a new lens is reproduced from the posterior epithelium of the iris. There are other observations of similar purport. The acceptance of this inference, however, seems to me to involve such difficulties that we may reasonably expect that further investigations will afford more satisfactory explanations of these curious and puzzling phenomena of regeneration. Of much interest and significance are the so-called atavistic regenerations, where the regenerated part assumes characters belonging not to the variety or species in which it occurs, but to some ancestral or allied species. For these and other reasons Driesch refers the pathological regenerations to what he calls the secondary self-regulations, by which term he designates those adjustments of artificially induced disturbances which are brought about by factors foreign to the normal development and life of the individual.

The view advocated by Barfurth seems to me more probable, that the pathological regenerations depend upon cellular properties pertaining to the normal life of the organism. This view is supported by the fact that, with a few probably only apparent exceptions, the regenerations conform to the law of specificity of cells. The pathological regenerations occurring after birth can be referred to the retention in greater or less degree of formative powers possessed by the cells pre-eminently in embryonic life. These powers in general tend gradually to diminution or extinction as the individual grows older, although in some cells, such as the covering epithelium of the skin and mucous membranes, this loss of regenerative power with advancing years is scarcely manifest. Even after the cessation of growth the regenerative capacity is not wholly in abeyance under physiological conditions. Bizzozero has studied and classified the various tissues of the body according to the activity of their physiological regeneration.

In general, the more highly differentiated and specialized a cell, the less is its capacity for regeneration; but we now know that such differentiation is attended with less sacrifice of its regenerative

power than was once supposed. Even such highly specialized cells as those of striped muscle are capable of regeneration. Indeed, the nerve-cells seem to be the only ones incapable of proliferation, and even this is not certain, for there are competent observers who claim that these cells may multiply, although there is no evidence that in the higher animals they can give rise to functionally active new nerve-cells. The ease with which a part of the nerve-cell, namely, its axis-cylinder process, can be regenerated is well known.

The cell-proliferation in regeneration is attributed to the removal of resistance to growth in consequence of the defect resulting from loss of tissue. It has been pointed out, especially by Ziegler and by Ribbert, that not only cells in the immediate neighborhood of the defect multiply, but likewise those at such a distance that it is difficult to suppose that the latter have been directly influenced by the loss of tension in the tissues caused by the defect. Ziegler refers the proliferation of the distant cells to compensatory hypertrophy, and Ribbert attributes it to hyperæmia resulting from the presence in the defect of foreign materials, such as extravasated blood, exudation, and necrotic tissue.

We are brought here, as we were in the consideration of the compensatory hypertrophies, to one of the most fundamental and important questions in pathology—the causes of pathological cell-growth. The interpretation of many pathological processes as adaptive or not, hinges often upon opinions held concerning the underlying causes of cell-proliferation. The main question at issue is: How far is one willing to go in attributing cell-growth to primary defects in the tissue, and interpreting the growth as for the purpose of regeneration or filling up a defect? Differences of opinion upon this subject are illustrated by the different interpretations of the cell-proliferations in acute and chronic inflammations, some pathologists considering these to be essentially regenerative and compensatory; others regarding them, at least in large part, as directly incited by inflammatory irritants and not to be ranked wholly with the regenerative processes.

The doctrine of Virchow was long accepted without question, that inflammatory cell-growth is the result of the action of external stimuli, the so-called inflammatory irritants, upon the cells, which are thereby directly incited to grow and multiply. The attack upon this doctrine has been most vigorously led by Weigert, who denies absolutely the power of any external agencies to stimulate directly cells to proliferation. He considers that to concede such a bioplastic power to external agents is equivalent to the acceptance of a kind of spontaneous generation of living matter.

Weigert's views upon this subject have undoubtedly had a most fruitful influence upon pathology. It has been such an influence as a good working-hypothesis, whether finally demonstrated to be true or not, has often had in the development of science. In putting to the test of actual observation Weigert's hypothesis, we have been led to recognize the frequency and the importance of primary injuries to cells inflicted by external agencies. Not only various degenerations and necroses of entire cells, but more subtle and partial damage of cytoplasm and nucleus have been made the subject of special study. It has been recognized that our older methods of hardening tissues reveal often only very imperfectly the finer structure of cells, and new and better methods have been introduced which enable us to detect more delicate lesions of cell-substance which formerly escaped attention, as is well illustrated in recent studies in neuropathology. Weigert's postulate of some primary injury to the tissues as the immediate effect of mechanical, chemical, and other external agencies, which were formerly regarded as the direct stimuli of cell-growth and multiplication, has been fulfilled in many instances where such damage had previously been overlooked or unsuspected. It is his belief that in cases where we cannot now detect such primary injury more thorough search and better methods will enable us to do so. One may, of course, reasonably cherish such an expectation; but at the same time we must recognize the fact that morbid cell-proliferations occur under circumstances where we cannot at present associate them with any demonstrable injury to the tissues—indeed, in some cases where our insight into the structure of the part seems to be so clear and satisfactory that one is very reluctant to admit the existence of an undetected damage to the cells.

Perhaps the most important modification of former pathological conceptions, resulting from the belief that cell-growth is caused by primary defects and injuries of tissue, relates to the chronic interstitial inflammations or fibroid processes. The older view that in these processes the active and essential feature of the disease is the new growth of connective tissue, which strangled the more highly organized cells of the part, has been replaced to a large extent by the opinion that the primary and most important lesion is the degeneration, atrophy, or necrosis of the more specialized cells, whose place is taken by the new growth of interstitial tissue. In many instances, as in fibroid patches in the myocardium, and in many scleroses of the central nervous system, this latter conception forms the best and most natural interpretation of the facts. There are,

however, great difficulties in explaining all chronic interstitial inflammations by this doctrine, and I must take side with those who admit the occurrence, for example, in the kidney and in the liver, of primary interstitial inflammations characterized by proliferation of the connective tissue and endothelial cells.

Indeed, it seems to me that Weigert's formula is too narrow to cover all of the observed facts concerning cell-proliferation. Essential features of the theory that cells cannot be directly stimulated to growth by external agents were present in Boll's doctrine of border warfare between neighboring cells. Weigert's presentation of this theory is in a far more acceptable shape than that of Boll. A still more comprehensive statement of the general theory is that cells are incited to growth through removal of obstacles to growth in consequence of some disturbance in the normal relations or equilibrium of the cells with surrounding parts. The capacity to proliferate must be present in the cells, but with the cessation of growth this capacity is rendered latent or potential by the establishment of definite relations or an equilibrium between cells and neighboring parts, including under the latter not only adjacent cells, but also basement-substance, lymphatics, blood vessels, tissue-juices, chemical substances, etc. It is evident that under these circumstances in only two ways can the cells be incited to growth, either by removal of resistance or obstacles to growth, or by an increase in the formative energy resident within the cell, and that in either way energy must be used, whether it be employed to remove obstacles to growth, or to increase the proliferative forces within the cell.

It appears to me by no means an easy matter to decide in all cases in which of the two ways mentioned cell-proliferation is brought about. Removal of obstacles to growth, not only in the way indicated by Weigert, but also by other disturbances in the neighborhood-relations of the part, and very probably by the presence of definite chemical substances, may be the explanation of all pathological cell-growths. Certainly it would not be easy conclusively to disprove this view. Nevertheless, I fail to comprehend the inherent difficulties which some find in admitting the possibility of forms of energy, acting from without, directly increasing the formative energy of the cell; in other words, directly stimulating the cell to growth and multiplication. If such a possibility be admitted, the natural interpretation of some examples of cell-proliferation is that they are directly caused by the action of external forces, in the sense advocated by Virchow.

Students of the problems of pathological cell-growth must take into consideration not only the facts of human and allied pathology,

but also those which are so rapidly accumulating in the domain of experimental embryology and morphology, to the importance of which I have repeatedly referred in this address. I would call attention especially to the observations from this source as to the influence of various changes of environment, particularly of definite chemical, thermic, and mechanical changes in surrounding parts, upon the direction of movement and of growth of cells. The use at present made of chemotactic phenomena in explaining the direction of movement of cells in human pathological processes is only a very limited and inadequate application of these important observations concerning tactic and tropic stimuli. We shall probably come to realize more and more the operation of these factors in determining cell-movements and cell-growth in human pathology. We already have evidence that different kinds of leucocytes not only possess different specific functions, but also respond in different ways to definite tactic stimuli. The long-standing problem of the lymphoid cell in inflammation approaches solution along these lines of investigation.

A burning question, and one of perennial interest, relating to our subject is: How far are we justified in regarding acute inflammation as an adaptive or protective morbid process? There is fair agreement as to the essential facts of observation, but regarding their interpretation there are wide differences of opinion, and when one considers the complexity of the process and its still unsolved riddles, it is not hard to see why this should be so. Much depends upon the point of view, and in this respect there can be recognized a certain antagonism between the purely clinical and the purely pathological and experimental views, an antagonism, however, which must be reconciled by a fuller knowledge of the subject.

It is not likely that the purely clinical study of inflammation would ever lead to the idea that the general tendency of this process is advantageous to the patient. The more severe and extensive the inflammatory affection, the more serious, as a rule, is the condition of the patient. The surgeon sees his wounds do well or ill according to the character and extent of inflammatory complication. Measures directed to the removal of inflammatory exudation, such as the evacuation of pus from an abscess or an empyema, are the most successful methods of treatment, and the rules are embodied in ancient surgical maxims. How can one conceive of any purpose useful to the patient served by filling the air-cells of his lung with pus-cells, fibrin, and red corpuscles in pneumonia, or bathing the brain and spinal cord in serum and pus in meningitis? If nature

has no better weapons than these to fight the pneumococcus or meningococcus, it may be asked, "What is their use but to drive the devil out with Beelzebub?"

But the pathologist and bacteriologist sees another aspect of the picture. An infectious micro-organism has invaded the tissues, where it multiplies and where its toxic products begin to work havoc with the surrounding cells, and by their absorption to cause constitutional symptoms and perhaps damage to remote parts. Is the destructive process to go on without any defence on the part of the body? There are attracted to the injured part an army of leucocytes from the blood vessels, and perhaps other cells, from the neighboring tissues, and it has been conclusively shown that these cells can pick up foreign particles and remove them, and that they contain substances capable of destroying many micro-organisms. At the same time serum accumulates in and around the injured area, and this may aid by its chemical properties in destroying bacteria, in diluting poisons, in flushing out the part. Fibrin may appear, and some think that this may serve in some situations as a protective covering. If these agencies, hostile to the invading micro-organism, gain the upper hand, the débris is cleared away by phagocytes and other means, and the surrounding intact cells, which had already begun to multiply, produce new tissue which takes the place of that which had been destroyed. The victory, however, is not always with the cells and other defensive weapons of the body. The struggle may be prolonged, may be most unequal, may cover a large territory, and the characters and extent of the inflammation furnish an index of these different phases of the battle.

Such in bald outlines are two divergent views of inflammation.

I do not see how we can fail to recognize in that response to injury which we call inflammation, features of adaptation. Inflammation may be in some cases the best response to secure the removal or destruction of injurious agents, but we cannot look upon it as the most perfect mode of protection of the body against invading micro-organisms. One may inoculate into three animals, even of the same species, but possessed of different individual resistance, the same quantity of the same culture of a pathogenic micro-organism and obtain sometimes the following results: The first one will present no appreciable inflammatory reaction whatever, and no evidences of any other disturbance, and examination will show that the micro-organisms have quickly disappeared. The second one will develop an extensive local inflammation and survive, but after a long illness. The third one will offer little resistance to the micro-organism, which rapidly multiplies without caus-

ing marked inflammation, invades the blood or produces toxæmia, and quickly destroys the life of the animal. Now, it is evident that the best protective mechanism is that brought into action by the first animal, but that the inflammatory reaction set up in the second one is better than the absence of reaction and of other defences in the third animal.

I can scarcely do more on this occasion than to indicate some of the points of view from which it seems to me that we can best approach the study of inflammation as an adaptive process. With inflammation, as with other adaptive processes, any useful purpose subserved affords no explanation of the mechanism of the process. We should guard against all ideas which introduce, even unconsciously, the conception of something in the nature of an intelligent foresight on the part of the participating cells. The response of these cells in inflammation is a necessary and inevitable one, determined by their innate properties. Our efforts should be directed, in the first place, toward as near an approach as possible to a mechanical explanation of inflammatory processes by a study, on the one hand, of the properties and mode of action of the causes of inflammation, and, on the other hand, of the nature and source of the cellular properties concerned. We may properly inquire whether these properties fit the cells to counteract the effects of injury, and if so, whence comes this fitness. Has the fitness those attributes of relative perfection which we find in most physiological adaptations? Is the character of the response to injury in inflammation such as to indicate that the agencies concerned have acquired through evolutionary factors a special fitness to meet the pathological emergencies? Are all or only a part of the manifestations of the inflammatory processes adaptive?

It cannot be doubted that there are innate properties of certain cells called into action in inflammation, such as those manifested in the attraction of leucocytes and other cells by definite chemical substances, the capacity of cell-proliferation from causes connected with injury, the power of phagocytosis and other bactericidal properties, which may be adapted to counteract the effects of injurious agents. When these forces bring about the prompt destruction or removal of the injurious substances and the defect is quickly repaired, the adaptation is complete and unmistakable. When, however, the inflammatory irritants and their destructive effects persist, and the proliferation of cells and accumulation of inflammatory products become excessive and occupy large areas, the features of adaptation are not so easily recognized. The mere occupation of territory by inflammatory products is often a serious injury and it

can be regarded as an adaptive feature only when they fill some artificial defect. Such occupation may be in itself enough to counteract any useful work in which these products may be engaged.

We can reasonably seek in the relations of the body to the outer world an explanation of the development of certain properties of cells which serve a useful purpose in mechanical and other injuries. These properties find application also in the normal life of the organism. Their exercise in response to injury imparts to inflammation important adaptive or protective characteristics, but I fail to see in this process any such special fitness as would justify extravagant statements which have been made, to the effect that inflammation ranks among the adaptations of living beings by the side of digestion and respiration.

I have endeavored in this address to present certain general considerations concerning pathological adaptations. It has been possible to bring under consideration only a small part of an immense field, and this very inadequately. We have seen that in the sense in which adaptation was defined we can recognize in the results of morbid processes frequent and manifold evidences of adjustment to changed conditions. These adjustments present all degrees of fitness. Some are admirably complete; more are adequate, but far from perfect; many are associated with such disorder and failures that it becomes difficult to detect the element of adaptation. The teleological conception of a useful purpose in no case affords an explanation of the mechanism of an adaptive process. I have suggested that the adaptability of this mechanism to bring about useful adjustments has been in large part determined by the factors of organic evolution, but that in only relatively few cases can we suppose these evolutionary factors to have intervened in behalf of morbid states. For the most part, the agencies employed are such as exist primarily for physiological uses, and while these may be all that are required to secure a good pathological adjustment, often they have no special fitness for this purpose.

The healing power of nature is, under the circumstances present in disease, frequently incomplete and imperfect, and systems of treatment based exclusively upon the idea that nature is doing the best thing possible to bring about recovery or some suitable adjustment, and should not be interfered with, rest often upon an insecure foundation. The agencies employed by nature may be all that can be desired; they may, however, be inadequate, even helpless, and their operation may add to existing disorder. There is ample scope for the beneficent work of the physician and surgeon.

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